# TROPICAL DISEASES BULLETIN

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

# TROPICAL DISEASES BULLETIN.

Vol. 43.] 1946. [No. 2.

## SUMMARY OF RECENT ABSTRACTS.*

## II. YELLOW FEVER.

### *Epidemiology.*

The Yellow Fever Research Institute at Yaba, Nigeria, was reopened in 1944, after having been practically closed since 1934. In the Annual Report (p. 800) it is explained that the Institute is financed as a joint venture by the Colonial Office, the West African Governments, and the Rockefeller Foundation. The work projected includes investigation into the epidemiology of the disease and the question of jungle yellow fever, and studies of the vectors. Yaba is to be the centre for the distribution and control of vaccine, and for protection tests. Precise instructions are given for the titration of vaccine. The authors point out that yellow fever in Africans rarely follows the usual textbook descriptions, and that the clinical concept should be broad.

DURIEUX (p. 275) gives an account of the yellow fever work done in French West Africa during 1942, when almost 3 million persons were vaccinated, either by inoculation or by scarification. The results of vaccinations performed in recent years, judged by protection tests, indicate that a large proportion of persons vaccinated remain protected for some years, but the fact that protection is not perfect is shown by the record of occasional deaths from yellow fever of persons previously vaccinated. Two such cases, in the 10 diagnosed during the year, are quoted and discussed. Most of these were apparently contracted in the jungle. In a later report (p. 723) he shows that by the end of 1943, at least half the population had been vaccinated by scarification, the vaccine being used either alone or mixed with smallpox vaccine. Protection tests, in which, however, the number of mice used is not given, have again indicated that protection is afforded in quite a high proportion of cases by this scarification method, but the remark is made that some people remove the vaccine before it has had time to penetrate the skin. Most of the 12 cases of yellow fever diagnosed in French West Africa during 1943 were related to a reservoir in wild animals, since the patients lived either in the bush or in very sparsely populated areas. CECCALDI (p. 802) reports on yellow fever in French Equatorial Africa, where two fatal cases occurred in Italian prisoners of war from the Tchad area.

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1945, v. 42. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

Elliott (p. 276) reports three cases of yellow fever in white soldiers in West Africa. All the patients had previously been vaccinated, but two of them died. Nevertheless, the low incidence of the disease is good evidence of the value of vaccination.

Kirk and Bayoumi (p. 374) report the first fatal case of yellow fever to be recorded in a European in the Sudan. Non-fatal European cases, some extremely mild, have been seen there before, and there have been many fatal cases in the Africans of the country.

### *Aetiology.*

Stéfanopoulo and Duvolon (p. 205) show that yellow fever virus, after prolonged maintenance in tissue culture, may undergo marked deterioration in both virulence and antigenic power. A strain of virus 17D which had become attenuated in this way was reactivated by passage through the brains of mice; it did not become pathogenic for monkeys, but produced immunity in them. After being cultivated in developing eggs, this strain was then used for vaccination of man, with success.

Jacobs (p. 465) has shown that in a mixture containing 10 per cent. human serum and 0·4 per cent. sodium chloride, to which is added ammonium sulphate to 1 per cent. strength, at *p*H 6·3–6·5, yellow fever virus remains viable, at 22–25°C., for as much as 20 days. Simple saline solutions are rapidly lethal to the virus, and the addition of serum is at best not very effective in preserving it.

Linhares (p. 277) shows that young cats are relatively insusceptible to yellow fever. He (p. 278) has been able to infect young mice by instilling the virus into the nostrils, the ear, on to the scarified cornea, into the stomach, or even by rubbing it into intact or scarified skin. The same author (p. 278) shows that chicks are susceptible to yellow fever virus injected by various routes, and that the virus persists longer in the brain than in the other organs. Virus may be present in the brain, and at the same time immune bodies may exist in the blood.

Linhares (p. 373) has found that filtrates of cultures of *Aspergillus flavus*, *Penicillium camemberti* and a species of *Actinomyces* have a lethal effect on the yellow fever virus, both *in vitro* and *in vivo*. A mixture of filtrate and virus is not pathogenic to mice, and injection of filtrate into these animals protects them against injection of virus several hours later. A non-infective mixture of filtrate and virus, however, possesses antigenic properties, and stimulates immunity.

### *Transmission.*

Corson (p. 597) has compiled, from the extensive literature on yellow fever transmission, a list of vertebrates tested for susceptibility to the virus, of invertebrates in which viscerotropic virus has been shown to persist, and of blood-sucking arthropods on which transmission experiments have been made. This list has been made as complete as possible, and brings the information up to date.

Hecht and Anduze (p. 465) give an account of the mosquitoes of Bolivar State, Venezuela, in so far as these may be concerned with the transmission of yellow fever. Special attention was paid to the jungle mosquitoes. [An examination of the table quoted by these authors from an earlier work, and showing the mosquitoes capable of transmission or in which virus has been found, reveals certain errors which have crept into the literature; see p. 640.]

Boshell-Manrique and Osorno-Mesa (p. 114) have demonstrated the existence of yellow fever virus in *Haemagogus capricorni* and (probably) *Aëdes*

*leucocelaenus* captured in uninhabited jungle in Colombia. Protective antibodies were found in certain marsupials. *Haemagogus capricorni* is attracted to light, travels considerable distances from its breeding places, and tends to follow man and mules some distance from the forest.

BEVIER (p. 557) contributes a report on the yellow fever service of British Guiana. No case was discovered in the year 1944. The supervision of aircraft and railway trains showed that there was a considerable transport of mosquitoes able to convey yellow fever and other diseases.

It is well known that *Aëdes aegypti* breeds in fire buckets, flower vases in cemeteries, drinking troughs and similar small collections of water. CHANDLER (p. 32) claims that phenothiazine is the ideal substance for control of such breeding, and that it may be applied as a powder, or incorporated in glue on small squares of paper which are placed in the water, or as a suspension in dilute alcohol. A single application in the proportion of 1 part to 60,000 of water will prevent breeding for three months or more.

HENDERSON (p. 374) describes the steps by which a high breeding rate of *Aëdes aegypti* in Savannah (on more than one-third of the premises) has been reduced so that it now occurs on no more than 2 per cent. of premises.

### *Immunity: Clinical Features.*

By a series of carefully planned experiments, LINHARES (p. 279) has shown that, in camondongos [Brazilian house rats], passive immunity (lasting 10 days or so) is transmitted from mother to young *via* the placenta and *via* the milk (lasting as long as lactation continues). Antibodies, therefore, pass through the placenta and also into the milk; there is no evidence that the virus itself does so.

PERLOWAGORA and LENNETTE (p. 114) have studied, in animals, the complement fixation reaction for yellow fever. The antigen for this reaction appears in the serum on the 3rd to 6th day after infection, but the antigen is not directly associated with the virus, which may exist in the absence of the antigen. The antibody is present in the serum of animals recently recovered from the disease. The test may be useful in diagnosis of human yellow fever. [For previous work by these authors on this test, in which antigen was obtained from infected mouse brain, see this *Bulletin*, 1945, v. 42, 83.] The same authors (p. 802) have found a correlation between the clinical severity of yellow fever and the amount of complement-fixing antigen in the blood, whereas there is no fixed relation between clinical severity and the amount of liver damage found after death. Moreover, the liver changes usually regarded as characteristic of yellow fever can be produced by injection of tannic acid, but without the formation of yellow fever virus antigen. The work indicates that the antigen is specific, and it was found in all the animals which had been infected with yellow fever. The complement fixation test, therefore, constitutes a more accurate and reliable method of diagnosis of yellow fever infection than the histopathological examination of tissue such as liver.

DE ASSUMPÇÃO (p. 277) discusses the differential diagnosis between yellow fever, dengue, Rift Valley fever, sandfly fever and leptospirosis. In spite of certain similarities—clinical and pathological features, transmission by *Aëdes*, production of lasting immunity—there is no cross-immunity between yellow fever and Rift Valley fever.

SELLARDS and MCCANN (p. 115) produce evidence that the oral administration of choline hydrochloride in monkeys infected with yellow fever has a protective action on the liver. Five of 8 monkeys so treated survived, whereas all of 4 controls died. There was evidence of repair in the livers of those treated monkeys which died.

*Control.*

In the Fourth Interim Report of the Inter-Departmental Committee on Yellow Fever Control (p. 721) are given recommendations concerning the most important measures of yellow fever control, especially with regard to suppression of *Aëdes* breeding near aerodromes, ports and other places on transport routes, the disinsectization of aircraft, the vaccination of travellers and those working at aerodromes, and the diagnosis of yellow fever. These should be read in the original. In the *Epidemiological Information Bulletin* issued by the Health Division of UNRRA (p. 890) are given the standards for manufacture and control of yellow fever vaccine ; these are stringent. They cannot further be abstracted, and details should be sought in the original.

HARGETT and BURRUSS (p. 803) describe their method of testing yellow fever vaccine by intracerebral injection into monkeys. The vaccine contains no serum and is attenuated, but in doses containing high virus content is capable of producing severe encephalitis in the monkeys. These monkey tests are a safeguard to man, and issue for human use is controlled by the results of the animal tests. No icterogenic or other untoward reactions have been recorded from batches released, after these tests, for use in man.

SPRAGUE and BARNARD (p. 890) report the cases of two men allergic to egg protein, who suffered severe reactions after the injection of yellow fever vaccine and typhus vaccine respectively. They advise that such persons should be excluded from the Services. *Charles Wilcocks.*

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## MALARIA.

OSGOOD, S. B. **Malaria and the Returning Soldier.** *J. Amer. Med. Ass.* 1945, June 16, v. 128, No. 7, 512–13.

Two persons, a white girl and a white woman, living in the State of Oregon, U.S.A., apparently contracted benign tertian malaria from a soldier who had returned from the Pacific area ; *Plasmodium vivax* was found in the blood in all three people. The girl and woman lived near a creek where mosquitoes were numerous but, according to the official records, no malaria had existed ; the soldier, who was related to the girl, had lived in a tent about 50 feet away from her house for over two weeks before she got the attack, and had often passed near the woman's house.

Mosquitoes caught near the girl's house were identified as *Anopheles punctipennis* and *Culex tarsalis*, and six specimens caught in the woman's house were *Anopheles maculipennis*. The presence of anopheline vectors of malaria in this neighbourhood had not been suspected.

There may have been a third case, in a logging partner of the soldier ; he was said to have had chills and fever but could not be found for examination. *J. F. Corson.*

MELVILLE, A. R., WILSON, D. Bagster, GLASGOW, J. P. & HOCKING, K. S. **Malaria in Abyssinia.** *East African Med. J.* 1945, Sept., v. 22, No. 9, 285–94, 1 map. [10 refs.]

A Mobile Malaria Section of the East African Army Medical Corps carried out malaria surveys in over 50 localities in Abyssinia during the British occupation of that country in 1941–42. Some of the results of these surveys are here recorded.

The Rift Valley traverses Abyssinia from the north of Lake Rudolf, northeastward to the Red Sea. *A. gambiae*, the chief vector, was found throughout

the valley. Other species of *Anopheles* found in the Rift Valley were : *A. coustani, A. obscurus, A. ardensis, A. kingi, A. d'thali, A. demeilloni, A. garnhami, A. macmahoni, A. christyi, A. cinereus, A. pretoriensis, A. maculipalpis, A. pharoensis,* and *A. squamosus.* Of these species only *A. pharoensis* and *A. d'thali* demand serious consideration as possible vectors. *A. pharoensis* is very common over wide areas, enters human dwellings and bites readily. The few dissections made revealed no sporozoites. This species was always found in association with *A. gambiae* and thus no circumstantial evidence was available as to its potentialities as a vector. *A. d'thali* is strongly suspect. It occurs in the Red Sea littoral. It was the only species found at Mordale (700 metres) where malaria occurs.

*A. gambiae* was found to be the vector of epidemic malaria in places in which mosquito breeding was dependent on rainy seasons. In other places the species was present throughout the year, breeding in residual pools left in river beds after torrents had subsided. In some of the smaller permanent rivers, pools and gently trickling water provide facilities for *A. gambiae* breeding.

As the level of the country falls from the plateaux of the east and west to the floor of the Rift Valley, malaria endemicity increases till a zone of moderate hyperendemicity is reached between 1,500 and 1,800 metres. At lower levels there may be intense hyperendemic malaria near streams, rivers or lakes, or low endemicity where rainfall is small ; in the latter places malaria is essentially seasonal.

Much of Abyssinia north-west of the Rift Valley is free from malaria, most of the country over 2,000 metres being too cold. There may be annual or periodic epidemics of malaria of some severity in this high country, but the endemicity and severity of epidemics are lower than in the Rift Valley. *A. gambiae* is the chief vector here also. At Jimma *A. funestus* was found in fair numbers after the rains and when the swamps had fallen in level. Other *Anopheles* found in the north-west were *A. coustani, A. kingi, A. nili, A. marshalli, A. harperi, A. demeilloni, A. christyi, A. cinereus* and *A. squamosus.*

South-east of the Rift Valley a massive mountain range forms the watershed of the Juba and Uebi Scebelli Rivers. East of this the land slopes to the low deserts of Somalia. Malaria occurs in varying degree along the slopes of the Chercher mountain range. Transmission is either absent or very brief at Harar (1,930 metres). There are highly endemic areas near Lake Chercher. At Negelli (1,290 metres) malaria transmission is slight and seasonal. Low endemicity characterizes the area including Mega, Moyale, Adola and Ghimir with the exception of the Dawa Parma and Ganale Doria river valleys, which are highly malarious. *A. gambiae* is the malaria vector in this south-east area. Other species found were *A. coustani, A. leesoni, A. rhodesiensis, A. demeilloni, A. cinereus* and *A. pretoriensis.* *Norman White.*

THOMSON, R. C. M. **Studies on the Breeding Places and Control of** *Anopheles gambiae* **and** *A. gambiae* **var.** *melas* **in Coastal Districts of Sierra Leone.** *Bull. Entom. Res.* 1945, Sept., v. 36, Pt. 2, 185–252, 8 text figs., 48 figs. on 13 pls. & 8 maps. [27 refs.]

*Anopheles melas* (for in the text the author accepts RIBBANDS's view that this is a species rather than a variety [this *Bulletin*, 1945, v. 42, 3]) differs from *A. gambiae* not only in the characters described by that author, but also in the egg. This has a broad upper surface with the space between the frill and the float so narrow that they appear to be in actual contact, instead of the narrow upper surface, with a distinct space wide enough to show the polygonal marking of the chorion between the frill and float in *A. gambiae.* The distinction of the

two species on the palpal bands is indefinite, *A. melas* sometimes having three and sometimes four bands and the proportion with each number varying from place to place.

The use of this characteristic has made it possible to identify with certainty the breeding places of the two species. *A. melas* is restricted to coastal areas and brackish swamps, very rarely making use of fresh water; of 2,647 eggs collected from fresh water unaffected by tides, only 30 were of the *melas* type, and these were found in places close to its normal breeding areas.

Breeding of *A. melas* is confined to the stretch of ground between high neap-tide and high spring-tide levels, and there only occurs in association with certain flora, *Avicennia nitida* mangrove and sea grass or *Paspalum*. Mangrove is of two types, the very common *Rhizophora racemosa*, with the well-known characteristic of roots like the stays of an inverted umbrella, and *Avicennia nitida*, which resembles an apple tree in appearance. The former is very much the commoner, and grows in mud below neap-tide level; the latter grows in scattered isolated "orchards," always above neap-tide and below high spring-tide level, on ground which is fairly solid and covered with a mat of leaves, but with many pools. On the extreme inland side of mangrove areas, of whichever type, there are often areas of sea grass which are inundated by extreme tides and which on account of their position tend to receive also fresh water from seepages as well as from rain. In *Avicennia* orchards, egg-laying takes place on the earliest of the spring tides, often only on the shore side of the orchard, and the eggs are distributed by the action of the tide, they and young larvae being undamaged by tidal water, which may flood the entire area to a depth of a couple of feet. On the subsidence of the spring tides some eggs are left in pools, in which they develop, others are stranded in mud, in which they survive until the next series of high tides floats them, when the eggs immediately hatch. In consequence the output of adults is highly periodic, occurring in waves a few days after the end of the spring tides. In *Paspalum* areas egg-laying may occur at any time, but is in fact often periodic as a reflexion of the varying numbers of adults available to lay. The periodicity and size of the output of adults is dependent on the following factors:—(*a*) the occurrence of spring tides; (*b*) the periodicity of the tides, as in a single month there may be either one or two series of sufficient height to flood the *Avicennia* orchards; (*c*) the occurrence of rain in sufficient amount to prevent the pools left by spring-tides from drying up before larval development is complete; and (*d*) the presence of seepages maintaining tidal pools, especially in *Paspalum* areas. These factors react together in different ways in different places and at different seasons, but, in general, output is greatest in the rainy season, particularly in June when it may be enormous, and continues until some months after the end of the rains, when seepages dry up, and reaches its lowest levels in the months of January to April. Although egg-laying only happens in coastal brackish water, a laboratory experiment suggests that it is not itself dependent on salinity, and the factor which causes this mosquito to choose this type of breeding place is not understood.

*Avicennia* orchards can be detected from the ground only with great difficulty. They are more readily detectable from above, from a nearby hill if such exists, or from aircraft. This last is the best method, as accurate mapping can be done by aerial photography, which has revealed only 17 orchards, many of them minor, in the enormous extent of general mangrove in the Freetown estuary. Control by drainage is not effective, as opportunity for egg-laying, and for the persistence of some breeding pools, inevitably occurs after spring tides. Control by embankment to exclude the spring tides from areas of *Avicennia* and *Paspalum*, associated with drainage of fresh water through tide gates, is much the most successful, and completely eliminates breeding.

A summary of dissections by another worker, and of which it is said that a detailed report will be published later, shows that 42 of 1,000 salivary glands contained sporozoites and 44 of 931 (4·7 per cent.) stomachs contained oöcysts, the total infection rate being 7·3 per cent.

*A. gambiae*, of the type form, breeds in fresh-water pools exposed to the sun. Detailed analysis of breeding places and of places not selected for breeding shows that this is only a small part of the story, and much remains obscure. Of the apparently suitable pools available, only a very small proportion are utilized, but these often contain very numerous larvae and continue to do so for long periods, and generalizations on breeding habits are impossible, or at least dangerous. In the general attack on a type of breeding place it is not uncommon to treat numerous water areas which are in fact harmless, and to overlook a few small ones which provide almost the entire local adult mosquito population. Breeding commonly occurs in small pools in sweet potato patches, and prolifically in rice fields at all stages of cultivation and throughout the entire season, but not throughout the entire extent of the field. In the rainy season profuse breeding occurs along the edge, often only a fraction of it ; in the dry season, though the water area is diminished, breeding becomes more widespread and the total output of adults may increase. Field trials show that oviposition is not influenced by light and shade, or by salinity below 30 per cent. of sea water, or by surface films caused by "iron bacteria" (though these films when continuous may prevent larval growth), but is influenced by mechanical obstruction interfering with the flight of the female before oviposition, as is the case with *A. culicifacies*.

*A. nili* has not in the past been regarded as an important vector of malaria in Sierra Leone, but it is here shown that in the dry season it may be the most abundant anopheline in some villages and may have very high sporozoite rates. Gordon *et al.* [this *Bulletin*, 1933, v. 30, 301] found a sporozoite rate of 9·1 per cent., and Tredre is reported as finding one of 3·2 per cent. It must, therefore, be considered as an important carrier of malaria.

[This paper contains much statistical and geographical information which cannot be adequately indicated in a review, and is illustrated by 50 photographs as well as by maps and plans. Any worker concerned in the control of *A. gambiae* in any part of Africa should try to see it in the original.]

*G. Macdonald.*

Delville, J. Infection naturelle d'*Anopheles demeilloni* par oocystes de plasmodium. [**Natural Infection of *A. demeilloni* with Plasmodial Oöcysts.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 112.

The author has found oöcysts (probably of *P. falciparum*) in one specimen of *Anopheles demeilloni* captured in Ruanda.

Cambournac, F. J. C. & Simões, J. M. P. Sôbre a produção de Anopheles nos arrozais de Aguas de Moura. [**The Production of *Anopheles* in the Rice-fields of Aguas de Moura.**] *An. Inst. Med. Trop.* Lisbon. 1944, Dec., v. 1, No. 2, 229–39, 2 graphs.

In a previous publication the senior author described his method for determining the larval *Anopheles* population of rice-fields [this *Bulletin*, 1939, v. 36, 920]. The interesting observations then reported have been continued during four successive rice-growing seasons and the results of those observations are here recorded. Malaria is hyperendemic in the Aguas de Moura district. *A. maculipennis atroparvus* is the only vector ; *A. claviger* also occurs, breeding

in clear cool water, but it is scarce and associates neither with human beings nor with domestic animals ; it is of no importance as a vector of malaria.

Breeding of *A. m. atroparvus* is at its maximum in May and June. There was considerable mortality among the larvae of all instars which did not appear to be due to an increase of their natural enemies. The proportion of the various instars in the total catch varied with great irregularity. The complete, or almost complete, absence of pupae after the end of June was a constant and striking phenomenon, though larvae in the fourth instar could be found. In the earlier months when pupae were found, their numbers had no constant relation to the numbers of fourth instar larvae. Though the production of adult anophelines ceases at the end of June, the number of these insects in catching-stations remains high throughout July and August. This indicates that the length of life of adult *A. maculipennis atroparvus* in natural conditions is from one and a half to two months.

It is estimated that at the height of the breeding season each hectare of rice-fields is capable of producing from 30,000 to 35,000 anophelines a day.

*Norman White.*

Eichler, W. Anopheles-Beobachtungen in Griechenland. [**Observations on the Anophelines of Greece.**] *Deut. Tropenmed. Ztschr.* 1944, June, v. 48, Nos. 11/12, 261–72, 9 figs.

Perret-Gentil, A. L'observation des réfugiés malariens dans la section clinique et le laboratoire de l'Institut Tropical Suisse. [**Study of Malaria among Refugees carried out in the Clinical Section and the Laboratory of the Swiss Tropical Institute.**] *Acta Tropica.* Basel. 1945, v. 2, No. 2, 97–121, 10 figs.

The arrival in Switzerland of a large number of Italian and Yugoslav refugees infected with malaria provided an opportunity for the staff of the Tropical Institute at Basle to undertake an intensive study of a disease that is rare in Switzerland. Very full advantage was taken of this opportunity. This paper records the results of the study of some 165 cases of *P. vivax* malaria.

Apart from the attacks of fever, characteristic symptoms were but little in evidence. Pain in the legs was a frequent complaint. Some temperature charts were very atypical. In about a quarter of the cases the fever was quotidian. Often a loss of weight heralded a relapse. In cases in which no parasites were found in the peripheral blood the injection of certain provocative agents sometimes yielded good results : adrenaline, milk, Caseosan and Pituiglandol were used for this purpose.

In the examination of blood a method is described which gave better results than the thick drop method. Four or five smears are superimposed, each smear being dried by waving the slide in the air before the next smear is spread.

Observations indicated that *P. vivax* has a greater affinity for mature red cells than for reticulocytes. Difficulty was sometimes experienced in differentiating the basophile stippling of red cells from Schüffner's dots in their early stage. Sternal puncture was not more successful in revealing parasites than was the examination of the peripheral blood. Henry's reaction was of little value.

In treatment, intravenous injections of quinine-calcium were often used without giving rise to any untoward symptoms : a preparation Calgluquine Sandoz in particular proved an active remedy that was well tolerated. Vitaquine Roche in tablet form gave results equal to those given by the usual quinine preparations.

*Norman White.*

Wilson, Margaret E. & Wilson, D. Bagster. **Malarial Infectivity in African Soldiers in a Hyper-Endemic Area.** *East African Med. J.* 1945, Sept., v. 22, No. 9, 295–7.

During a period of six months thick blood films were taken fortnightly from 137 African soldiers who were being exposed to frequent reinfection by alien, if not new, strains of malaria parasites. The results of the examination of these films are recorded. None of the men was sick when the films were taken. The men belonged to a large variety of tribes and most had a considerable degree of immunity to malaria. They were classified as : immune, 76 ; semi-immune, 42 ; non-immune, 19.

The average parasite rate at these examinations was 16·1 per cent., *P. falciparum* 14 and *P. malariae* 2·1 per cent. Crescents were counted against leucocytes or, when very few, recorded as one or two in the whole thick film. Only three crescent carriers were found with counts of over 10 per 500 leucocytes, two of them being of non-immune tribes. Eight had counts of 1–4 per 500 leucocytes. Twenty-eight crescent carriers had counts of less than one per 500 leucocytes. On the assumption that at least one crescent per 500 leucocytes is necessary for successful mosquito infection, not more than 1 per cent. of these soldiers at any one time was a probable infector. Half of these infectors belonged to the non-immune group, which formed but one-seventh of the men examined. *Norman White.*

Fredericks, M. G. & Hoffbauer, F. W. **A Study of Hepatic Function in Therapeutic Malaria.** *J. Amer. Med. Ass.* 1945, June 16, v. 128, No. 7, 495–8, 4 charts. [13 refs.]

Thirty-one patients subjected to malaria therapy are the basis of this report, 21 men and 10 women between 28 and 62 years of age. All suffered from acquired neurosyphilis. *P. vivax* was inoculated intravenously in 29, intramuscularly in 2. No manifest liver disease was noted in any of these patients before submission to malaria therapy. All but six of the patients received general diets ; the six received liver-sparing diets, high carbohydrate, high protein and low fat.

Among the clinical features recorded were : loss of weight ; symptoms and signs of gastrointestinal disturbance ; degree of weakness. Hepatic disturbance was assessed by the quantitative serum bilirubin test ; the cephalin cholestrol flocculation test ; the amount of urobilinogen in the urine, and the sulphobromophthalein dye retention test. The technique of these tests is briefly described. The results obtained are recorded in the form of graphs.

All the patients showed some evidence of hepatic dysfunction ; there was jaundice in one patient, enlargement of the liver in four and spider naevi in five, symptoms which correlated with the hepatic disturbance revealed by liver function tests. The weight loss during and immediately after malaria therapy was striking ; this can be lessened but not prevented by special diet. More attention should be given to the study and use of protective diets during malaria therapy. Such therapy is admittedly contraindicated in the presence of clinically manifest hepatic disease. *Norman White.*

Chen, K. T., Tang, I. L. & Wang, M. C. **Congenital Malaria. Report of a Case.** *Chinese Med. J.* Washington, D.C. 1944, Apr.–June, v. 62, No. 2, 199–205.

Marshall, P. B. **Loss of Antimalarial Properties in Quinine Degradation Products.** *Nature.* 1945, Oct. 27, 505–6.

A degradation product of quinine was obtained by Kelsey *et al.* [this *Bulletin*, 1944, v. 41, 923] following incubation of the alkaloid with rabbit

liver *in vitro*. It was shown by MEAD and KOEPFLI [this *Bulletin*, 1945, v. 42, 9] to be a simple derivative of quinine in which the H atom at position 2 of the quinoline nucleus was replaced by a hydroxyl group. The present author has investigated the action of the degradation product on *P. gallinaceum* infections of chickens. In one incubation experiment half the rabbit liver emulsion with quinine was treated with alkali, in order to destroy enzymatic activity, the other half was untreated. The chloroform extract of the former contained unchanged quinine, the latter did not. Both extracts, made up in HCl, were used in the treatment. The antimalarial activity of the pure degradation product in dilute HCl was also compared with that of a corresponding dose of quinine. It was found that the above extract in which all the quinine had been metabolized, as well as the degradation product isolated in the pure state, failed to reduce the number of parasites in the peripheral blood of the chickens. [SILVERMAN *et al.* (this *Bulletin*, 1945, v. 42, 448) found, on the other hand, that it was as effective as the parent substance in inhibiting the respiration of the same parasites *in vitro*, but affected aerobic and anaerobic glycolysis to a lesser degree.] The author notes that whereas quinine and quinidine are metabolized in the same way, cinchonine and cinchonidine are not metabolized by chick liver suspensions. This fact may be of some significance in preparing new antimalarial products of related type.

*J. D. Fulton.*

MARSHALL, P. B. & ROGERS, E. W. **A Colorimetric Method for the Determination of Cinchona Alkaloids.** *Biochem. J.* 1945, v. 39, No. 3, 258–60, 2 figs.

"1. A colorimetric method for determining cinchona alkaloids, based on the formation of a coloured compound with bromothymol blue, is described.

"2. Using small capacity cells in a photoelectric photometer, the method is sensitive to 0·25 $\mu$g. of alkaloid.

"3. The specificity of the reaction has been investigated, and lists of substances which do or do not combine with bromothymol blue are included."

THOMPSON, J. H. **Large Initial Doses of Atebrine in the Treatment of Benign Tertian Malaria.** *J. Trop. Med. & Hyg.* 1944, Dec.–1945, Jan., v. 47, No. 6, 61–4.

One hundred American soldiers who had acquired *P. vivax* infections in the Mediterranean area during 1943 were treated for relapsing malaria in England during the following March and April. Seventy-eight of these patients received an initial dose of 0·6 gm. of mepacrine, followed by 0·2 gm. after each meal for six doses, and then 0·1 gm. thrice daily after meals for 7 days. The remaining 22 patients received 0·2 gm. of the drug every four hours for five doses and then 0·1 gm. thrice daily for 5 days. All the mepacrine was given by mouth in the form of 0·1 gm. tablets : it was always given after meals. If the initial dose was given between meals it was preceded by a pint of chocolate, milk, fruit juice or egg nog.

Of the 78 patients who received the large 0·6 gm. initial dose of mepacrine, three (4 per cent.) relapsed between 14 and 30 days after completion of treatment. Five (23 per cent.) of the 22 patients on the smaller doses relapsed during the same period of observation. In none of the 100 patients were there toxic symptoms severe enough to necessitate modification of the treatment. Fifteen per cent. had mild abdominal cramp after the initial 0·6 gm. dose ; 6 per cent. had mild diarrhoea.

The eight patients who relapsed were subsequently treated with still larger doses : an initial dose of 1 gm. followed by 0·2 gm. every 4 hours for 6 doses and then 0·1 gm. thrice daily for a week. This very large initial dose was

given 24 hours after the second or third chill. In four of the cases serial blood smears were taken every 45 minutes after the initial dose. Clumping of the pigment in plasmodia was seen as early as 45 minutes after the initial dose; thereafter disintegration became progressively more marked, and after about 6 hours destruction was complete. About 6 hours after the 1 gm. dose the patients experienced a very violent chill, the last and only one. Toxic effects were more in evidence than after the 0·6 gm. dose. Four patients had nausea, one vomited, one had marked diarrhoea and one had mental symptoms. The delirium of the patient with mental symptoms was transitory and may have been due to the fever or mepacrine or both. *Norman White.*

Ann. Trop. Med. & Parasit. 1945, Oct. 10, v. 39, No. 2, 128–32. **Prolonged Oral Administration of Mepacrine. I. The Effects on Tests of Organ Function.** [The Army Malaria Research Unit, Oxford (Maegraith, B. G. *et al.*).]

Forty-three healthy young male adults were given mepacrine 0·1 gm. daily. At the beginning of this study careful biochemical examinations were made on each individual. The examinations were repeated at intervals of approximately three months until the end of the experiment, which lasted between 9 to 12 months. The findings in the later tests were compared with those of the initial tests and with those obtained with 13 similar subjects who received no drug. No significant change could be observed in the following:—icterus index, serum bilirubin, fasting blood sugar, glucose tolerance, fructose tolerance, blood urea, urea clearance, hippuric acid synthesis, total plasma protein, albumin globulin ratio in the plasma, plasma fibrinogen, Takata-Ara test, blood chloride, or qualitative examination of the urine. It is concluded that there is no evidence that this course of mepacrine impairs the efficiency of the liver or kidney. [A brief account of these experiments was published in the *Lancet*, 1945, Aug. 4, 141 (see this *Bulletin*, 1945, v. 42, 863).]

*F. Hawking.*

Ann. Trop. Med. & Parasit. 1945, Oct. 10, v. 39, No. 2, 133–6. **Prolonged Oral Administration of Mepacrine. II. Haematological Effect.** [The Army Malaria Research Unit, Oxford (Maegraith, B. G., *et al.*).]

Sixty-five women and 30 men (all healthy young adults) were given mepacrine in a dosage of 0·4–0·7 gm. weekly for 4–10 months. During this period there was no significant change in the red-cell count, the white-cell count, the haematocrit or the erythrocyte sedimentation rate. A small rise in haemoglobin concentration occurred in the men taking mepacrine, and also in a control group of 14 men who received no drug; this apparent rise may have been due to some alteration in the standard used for measurement rather than to any true physiological change. It is concluded that this dosage of mepacrine for long periods has no deleterious haematological effect. [See this *Bulletin*, 1945, v. 42, 863.] *F. Hawking.*

Gahan, J. B. & Lindquist, A. W. **DDT Residual Sprays applied in Buildings to control** *Anopheles quadrimaculatus*. *J. Econom. Entom.* 1945, Apr., v. 38, No. 2, 223–30.

——, Travis, B. V., Morton, F. A. & Lindquist, A. W. **DDT as a Residual-Type Treatment to control** *Anopheles quadrimaculatus*: **Practical Tests.** *Ibid.*, 231–5.

——, —— & Lindquist, A. W. **DDT as a Residual-Type Spray to control Disease-Carrying Mosquitoes: Laboratory Tests.** *Ibid.*, 236–40.

This series of papers constitutes a full enquiry into the efficacy of DDT for the control of adult *Anopheles quadrimaculatus*, starting with laboratory

experiments and passing on to small field trials and then to large scale field work.

In the laboratory trials cages of various materials were treated with known quantities of DDT, anophelines subsequently liberated into them, and the knock-down and mortality studied. The knock-down was noted hourly for the first five hours and the final mortality was recorded at 24 hours. Preliminary trials showed that *Anopheles quadrimaculatus* and *Aëdes aegypti* were about equally susceptible, and anophelines only were, therefore, used in later tests.

The concentration of chemical in the spray used does not materially affect the toxicity of the residue if the deposit is the same, and 2·5 per cent. DDT was used as the standard. The nature of the vehicle did affect its toxicity to some extent, emulsions and suspensions being about equal to each other and a little better than kerosene solutions. The lethal effect was slow and exposures of 2 to 4 hours were required to give kills approaching 100 per cent. in the case of newly applied films, and as long as 4 hours in the case of older films. The exposure time required for complete mortality was the same 17 weeks after sprays had been applied, and increasing the amount of DDT from 50 to 400 mgm. per sq. ft. of surface did not decrease the time.

Unpainted surfaces treated with the chemical remained lethal for long periods, in some cases as much as a year, but the knock-down time slowly increased during this time from about 2 hours to 5 or more hours in films 32 weeks old. On painted surfaces a 100 per cent. kill was recorded 32 weeks after 50 mgm. per square foot had been applied to surfaces coated with cold water casein paint. The duration of effect was, however, much shorter on surfaces recently treated with oil paint, mortalities below 100 per cent. being recorded when the film was a week old, and the knock-down after 5 hours being reduced to 25 per cent.

Exposure of treated surfaces to sunlight reduced the length of time for which they were effective by about half, and experiments to determine whether mosquitoes left the treated surfaces before they had received a lethal dose showed that the great majority died within 24 hours of voluntarily leaving surfaces treated in this way.

In the field trials, rooms were treated with known doses and the effect on artificially introduced or naturally entering anophelines was studied, the dose was varied from 50 mgm. up to 225 mgm. per square foot and resulted in a reduction of the anopheline population to about 4 per cent. of that in control rooms. The duration of effect could not be studied owing to a natural decrease in the control rooms four weeks after the experiment was started. Mosquitoes attempting to leave the rooms were captured and 95 per cent. of those leaving died within 24 hours.

The authors also studied the biting rate of anophelines not yet knocked down in treated rooms, and found that this was about proportional to the numbers surviving in the room, and concluded that obvious contact with DDT does not act as a deterrent to biting.

In the large field trial, two areas each of about 9 square miles were selected in rice growing country, and all buildings, bridges, culverts and other possible shelters were treated. In the one the average dose was 56 mgm. per sq. ft. and in the other 208 mgm. per sq. ft., and adjacent similar areas served as controls. The object was to see if the general anopheline population in the vicinity of sprayed buildings, as well as in the buildings themselves, could be reduced by the use of residual sprays without employing other methods, and this was studied by counting anopheline adults in the treated houses and in nail kegs, left as traps throughout the area, and also by estimating the numbers of larvae in local breeding places.

The anopheline counts in houses for four months following the end of treatment are recorded in detail, and when compared with adjacent control areas showed a reduction of 91 per cent. where 56 mgm. per sq. ft. had been applied, and of 99 per cent. where 208 mgm. had been used. The counts were normally made in the afternoons when mosquitoes would have been in contact with treated surfaces for several hours, the few counts made in the early morning showed a smaller relative reduction, but as the great majority of captured adults died in 24 hours it may be assumed that these only reflected the previous night's hatch.

The catches in the artificial traps showed no difference between the treated zones and the controls. There were, however, a number of confusing factors affecting these results and it is not to be taken as proven that there was no reduction in the general mosquito density.

Estimation of the numbers of larvae in breeding places in treated and controlled zones was done by a dipping technique at weekly intervals after the experiment had started. In each of the 20 counts recorded there was a reduction in the treated area which, when compared with the controls, amounted to 51 per cent. in the zone where 56 mgm. were used, and 63 per cent. in the zone where 208 mgm. had been applied. In each case the number of small, medium and large larvae was recorded, and it is noticeable that the reduction of large larvae was less than that of small ones. *G. Macdonald.*

Deonier, C. C., Maple, J. D., Jones, H. A., Hinchey, Edna & Eide, P. M. **DDT as an Anopheline Larvicide—Laboratory Tests.** *J. Econom. Entom.* 1945, Apr., v. 38, No. 2, 241–3.

——, Burrell, R. W., Maple, J. D. & Cochran, J. H. **DDT as an Anopheline Larvicide : Preliminary Field Studies.** *Ibid.* 244–9.

Wisecup, C. B. & Deonier, C. C. **DDT for the Control of *Psorophora* Mosquitoes.** *Ibid.* 250–52.

This series of papers constitutes an enquiry into the effect of DDT as an anopheline larvicide, starting with laboratory tests and going on to field studies.

In the laboratory tests early fourth instar larvae of *Anopheles quadrimaculatus* were used and mortality readings were made at 24 and 48 hours after application of the larvicide. In some cases the tests were continued for long periods, new larvae being introduced periodically and the effect of rain artificially simulated.

The minimum lethal dose of acetone water suspensions of DDT could not be accurately determined, but 98 per cent. mortality was seen at a concentration of 0·01 parts per million, 55·5 per cent. at 0·005 p.p.m., and some toxicity was shown at 0·00125 p.p.m. It was found to be about 100 times as toxic as phenothiazine and more rapid in action. When applied as a dust and compared with Paris green it was found that doses of 0·005 lb. DDT per acre gave 100 per cent. kill in 48 hours, while 0·1 lb. Paris green per acre only gave 85 per cent. kill in the same period. DDT had the additional great advantage that it was very resistant to sinking, either naturally or after rain ; its resistance was always obvious, but to some extent depended on its physical form, " micronised " DDT surviving 14 to 20 rains, while non-micronised DDT, which would pass a 200-mesh screen, was rendered ineffective by three periods of rain. It also depended to some extent on the vehicle, as solid solutions in calcium stearate and stearic acid gave the best results, a mortality above 80 per cent. being obtained after 86 days with 44 artificial rains. Mixtures with talc were effective for 30 days with 16 rains, and those with stearic acid for 38 days with 20 rains.

Laboratory trials were also made of oil solutions applied as a film, when 0·05 to 0·1 lb. per acre were effective, and of emulsions and suspensions with which 0·01 p.p.m. were effective for 8 to 10 days.

Field trials with dusts showed that 0·05 to 0·1 lb. per acre gave 100 per cent. kill but had no residual action. To secure this residual effect 1 to 2 lb. per acre had to be applied, usually in the form of a 20 per cent. mixture with the vehicle. The duration of the effect varied with the type of water, being longest (up to 8 or 10 weeks) where thick surface vegetation prevented the dusts from being blown to one side, and least in the presence of sparse vegetation, where application was again necessary two weeks after the first dusting.

Solutions in petroleum oils were less satisfactory than dust mixtures, and, mainly owing to the difficulty of getting good coverage of the area with the oil film, the effective dose was 0·1 lb. per acre and the resulting kill varied from 75 to 100 per cent., being usually over 90 per cent.

Two types of suspension were used ; in one, DDT was in colloidal solution in the water, and in the other it was in solution in xylene which was itself dispersed in colloidal-sized droplets ; they showed very high promise and gave 94 to 100 per cent. kill which remained apparent for as long as three months. It is noted, however, that at high concentrations these suspensions were toxic to cold-blooded animal life, and killed fish, frogs and snakes as well as aquatic insects.

Large field trials were made with the object of controlling *Psorophora* mosquitoes, the adult females of which lay their eggs in places liable to flood. Hatching of the egg occurs when the area is flooded and is followed by a very short aquatic stage. Two techniques were tried, in the one, the soil liable to flood and containing eggs was treated, in the other, surface applications were made to the water after the flood had occurred In the first technique the application of DDT as a dust was ineffective, but the application of solutions and emulsions at the rate of 0·1 lb. per acre at the first flood gave perfect results. Experiments were also made with a self-operating dispenser which released DDT solution automatically when the flood happened, and this also was found effective.

Surface applications of 0·1 lb. DDT per acre by dusting, pouring of oil, spraying of oil or xylene emulsions, or by using impregnated sawdust gave control, and in this case there was some indication of a residual action at the second time of flooding. *G. Macdonald.*

Metcalf, R. L., Hess, A. D., Smith, G. E., Jeffery, G. M. & Ludwig, G. W. **Observations on the Use of DDT for the Control of** *Anopheles quadrimaculatus*. *Pub. Health Rep.* Wash. 1945, July 6, v. 60, No. 27, 753–74, 1 text fig. & 4 figs. on 4 pls.

The median lethal doses of DDT and pyrethrins to laboratory-reared *Anopheles quadrimaculatus*, as shown by tests in a Peet Grady chamber, are :—

| | $LD_{50}$ in milligrammes per 1,000 cu. ft. | |
|---|---|---|
| | Males | Females |
| DDT ... ... | 7·0 | 12·0 |
| Pyrethrins ... | 1·0 | 1·5 |

When tested as a residual insecticide, doses of 40, 200 and 1,000 mgm. per sq. ft. showed no significant differences in initial toxicity, the percentage mortality being determined by the period of contact of the mosquito with the treated surface, which suggests that some physiological reaction, such as the rate of absorption, limits its action. Surfaces treated with heavy doses retain

their toxicity, however, for a longer period than do those which have received smaller doses, a fact which was confirmed in laboratory and field tests. In the former a 60-minute contact of female *A. quadrimaculatus* with films of different strengths and ages produced the mortalities shown below :—

| Age of Film | Dose of DDT in milligrammes per square foot | | |
|---|---|---|---|
| | 40 | 200 | 1,000 |
| | Per cent. | Per cent. | Per cent. |
| New ... ... ... ... | 100 | 100 | 100 |
| 1 week ... ... ... | 100 | 100 | 100 |
| 2 weeks ... ... ... | 100 | 100 | 100 |
| 4 weeks ... ... ... | 100 | 100 | 100 |
| 8 weeks ... ... ... | 20 | 71 | 100 |
| 12 weeks ... ... ... | 44 | 62 | 100 |
| 16 weeks ... ... ... | 0 | 22 | 30 |

Males were more readily killed than females, and shorter periods of contact showed the same general effect of ageing of films. In field experiments the toxicity of films of 20 mgm. per sq. ft. dropped below a useful level after about 18 weeks, and this loss of toxicity appeared to be mainly due to crystals flaking off the surface rather than to volatilization. Vibration, as in ordinary occupation of a house, accelerates this effect.

Practical trials were made of an emulsion consisting of a 1 in 4 dilution of a stock concentrate of 25 per cent. DDT, 7 per cent. Triton (emulsifier), and 68 per cent. xylene, applied by means of a portable hand spray, with which two men could treat about 20 houses per day. Direct measurement of the efficacy was made difficult by the small numbers of mosquitoes in control houses, but liberation of adult mosquitoes into the houses showed that the films remained effective for the remainder of the season, the period required for complete knockdown in an inhabited house 8 weeks after treatment being 230 minutes. It was noted that smooth enamelled or smooth papered surfaces lost their toxicity more rapidly than rough wallboard.

Both in houses and experimental kegs left in the open it was noted that those treated with DDT exerted a definite repellent effect, and in newly treated houses there was a marked decrease in the biting rate despite the entry of mosquitoes, an effect which decreased, however, with the ageing of the films. It appeared that DDT does not deter mosquitoes from entering a treated room, but exerts an irritant effect after they have been in contact with a treated surface for a short time. However, at least 95 per cent., and probably almost 100 per cent., receive a lethal dose before leaving houses and the chain of malaria transmission is thereby effectively broken.

Emulsions of DDT solutions in kerosene were effective larvicides when the dose of DDT amounted to 0·1 lb. per acre of water surface. Some difficulty was met in applying powdered DDT from aircraft owing to caking of the substance when its concentration in inert dust exceeded 5 per cent. With dust dilutions of this nature, 90 per cent. larval control was obtained over 200 foot swaths at actual application rates as low as 0·05 lb. per acre, but this involved carrying a heavy load of inert dust and thereby counterbalanced any advantages gained by applying DDT in this form. The spraying of kerosene solutions from aircraft also presented some technical difficulties and an unduly high pay load, so that the authors turned to 15 to 40 per cent. solutions of DDT in "certain polymethylnapthalenes" which, when sprayed from a specially developed apparatus on a Stearman plane, gave 90 per cent., or better,

kills over a swath 200 to 300 feet wide, at doses of DDT of less than 0·03 lb. per acre. Considerable trouble was spent on the development of thermal generators, DDT solution being discharged into an extension of the exhaust, and an apparatus was finally devised which produced a visible aerosol, 90 per cent. of the droplets in which were between 5 and 100 microns in diameter ; this was satisfactory and gave 90 per cent. larval kills over a swath 300 feet wide at application rates of 0·04 lb. per acre. It was also very effective in killing adult mosquitoes, both caged and wild, even when protected by dense woods, though for this purpose a dose of 0·4 lb. per acre was needed. Aerosols of this nature were much superior, for this last purpose, both to smokes with finer droplets, and to coarser sprays. Another advantage of this type of application was that it was much less toxic to other aquatic insects than the application of kerosene solutions. *G. Macdonald.*

Simmons, S. W. & Staff. **Tests of the Effectiveness of DDT in Anopheline Control.** *Pub. Health Rep.* Wash. 1945, Aug. 10, v. 60, No. 32, 917–27, 3 figs.

The value of DDT as a residual spray has been tested in a series of field and laboratory experiments, the scale of which can be estimated from the fact that 33,000 adult *Anopheles quadrimaculatus* have been used in 1,800 individual tests, and the main results of which are well illustrated in graphs showing the rate of knock-down of mosquitoes exposed to films of different ages, the comparative values of various solutions and emulsions, and the comparative values of various doses of DDT. The first follows the now generally accepted pattern of slower knock-down with increased age of film. The least effective vehicle was a Lethane water emulsion, which gives an amorphous deposit probably covered by a protective film of the solvent. The most satisfactory emulsion was a 35 per cent. solution of DDT in a light proprietary oil known as PD544 C, emulsified in water with 4 per cent. " Triton X-100 " in xylene, 4 per cent. " Duponol OS," or 0·5 per cent. " Arctic Syntex A " as emulsifying agents. Emulsions in which the dispersed phase was cylene or cyclohexanone were slightly less effective, and about equal to kerosene solutions. [It would appear, though not certainly, that these tests were carried out on unpainted wood panels. Other recent work suggests that kerosene solutions are much less effective against flies on painted surfaces.] An interesting note is made of the crystal shapes resulting from application in different vehicles, which may throw some light on this varying effect. Kerosene solutions leave long, fragile, needle-shaped crystals ; crystals from emulsions are on the whole smaller, in some cases less fragile and more compact, while Thanite and Lethane leave amorphous deposits which may be covered by a protecting film of the solvent.

The effect of varying the dosage of DDT is to vary the minimum period of contact needed to secure 100 per cent. mortality, but as a practical point it seems that films ten weeks old, varying from 50 to 300 mgm. per sq. ft., give about the same mortality amongst mosquitoes exposed to them for 60 minutes, though after the ten-week observation period the 50 mgm. dose may lose toxicity earlier than the 100 mgm. dose.

The overall cost of treating the average tenant house (1,700 sq. ft. of wall and ceiling surface) with a DDT-xylene-Triton-water emulsion at a dose of 200 mgm. per sq. ft., varied from $1.50 to $1.75, and this low cost is considered to presage a degree of malaria control not previously obtainable. A series of releases of 600 to 2,000 mosquitoes in treated rooms showed that this dose was still effecting a complete kill after 22 weeks.

When applied at a dose of 0·1 lb. per acre, either in surface films, emulsions, or suspensions, DDT will kill all anopheline larvae within 24 hours. The technique used was to prepare emulsions, or other vehicles, of such a strength that a total quantity of 15 to 20 gallons per acre gave the required dose of 0·1 lb., and considerable saving was thus achieved in material costs compared with oil [but not in labour costs]. In making surface films, an emulsion of DDT/oil solution was made in water, using an emulsifying-spreading agent [1·25 per cent. DDT, 0·5 per cent. " B-1956 (an emulsifying-spreading agent) " in No. 2 fuel oil, of which one gallon is mixed with 15 to 20 gallons water]. A type formula for emulsions was DDT 35 per cent. in xylene with " Triton X-100," " Duponol OS," or comparable emulsifiers, and suspensions were prepared by dissolving the DDT in a water-miscible solvent such as alcohol and adding to water with a dispersing agent.

From 90 to 95 per cent. of the kill takes place within the first hour after treatment, and the residual effect wears off within a few days, though the subsurface water, when abstracted and tested in the laboratory, remains toxic to larvae for a rather longer period. DDT has virtually no effect on plankton and some larger forms of life such as *Daphnia*. When the dose is considered, not in relation to the water surface, but in relation to its volume, quantities between 0·02 and 0·2 parts per million have very similar effects.

The ultimate destruction of the DDT seems to be the result of action by the bottom mud complex, as laboratory trials show that destruction takes place much more rapidly in its presence than in its absence. *G. Macdonald.*

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## TRYPANOSOMIASIS.

HARDING, R. D. **Late Results of Treatment of Sleeping Sickness in Sierra Leone by Antrypol, Tryparsamide, Pentamidine, and Propamidine, Singly and in various Combinations.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Oct., v. 39, No. 2, 99–124.

This is an account of the effects of treatment, followed for 13 to 28 months (in a few instances up to 46 months), in 2,713 cases of sleeping sickness in the Kailahun District of Sierra Leone. A report on the earlier results of treatment in a large proportion of these cases has already been published [this *Bulletin*, 1943, v. 40, 370]. Deaths since the start of treatment totalled 228 (of which 181 were attributed to sleeping sickness or the toxic effects of the drugs employed), and only 126 cases remained untraced.

The courses of treatment employed were as follows :—

(i) Antrypol, five doses of 1 gm. at 5-day intervals in cases with a normal cerebrospinal fluid cell count.

(ii) Tryparsamide, six to ten doses of 2 gm. at 5-day intervals. The majority of patients received nine or ten doses.

(iii) Antrypol, three doses of 1 gm., followed by tryparsamide, three to five doses of 2 gm. all at 5-day intervals.

(iv) Three other combinations of antrypol and tryparsamide designed to reduce the toxicity exhibited by Course iii :—

  (*a*) Antrypol, three doses of 1 gm., followed by tryparsamide, three to seven doses of 2 gm. An interval of 5 or 7 weeks separated the first and second doses, the remainder being given at 5-day intervals.

  (*b*) Antrypol, two doses of 1 gm., followed by tryparsamide, four to six doses of 2 gm., at 5-day intervals.

  (*c*) Antrypol, one dose of 1 gm., followed by tryparsamide, eight or nine doses of 2 gm., at 5-day intervals.

(v) Pentamidine, eight to twelve doses of 50 to 100 mgm. daily.

(vi) Propamidine, eight doses of 50 to 75 mgm. daily.

The remaining three courses constituted a small-scale trial of a combination of pentamidine and tryparsamide administered concurrently :—

(vii) Pentamidine, five doses of 100 mgm., and tryparsamide, five doses of 2 gm., at 5-day intervals. On each treatment-day both drugs were given, the pentamidine first, and tryparsamide about two hours later.

(viii) Pentamidine, five doses of 100 mgm. daily, and tryparsamide, five doses of 2 gm. at 5-day intervals. Tryparsamide was given on the first treatment-day, pentamidine on the 2nd to 6th days inclusive, and tryparsamide again on the 7th, 12th, 17th and 22nd days.

(ix) Tryparsamide alone, five doses of 2 gm., at 5-day intervals, to serve as a control for Courses vii and viii.

Cerebrospinal fluid cell-counts had been made before treatment in 1,170 cases, in 579 of whom this examination was repeated, usually together with an estimation of total protein, at the final follow-up. Cerebrospinal fluid was also examined, at the final follow-up, in 383 other patients in whom lumbar puncture had not been performed at the start of treatment.

The author discusses the relative importance of various criteria in assessing the results of treatment :—

(i) *Clinical condition.*—This is regarded as unreliable, since some patients with considerably raised C.S.F. cell-counts may appear quite well, whilst others with normal counts may present symptoms which superficially suggest relapse, but which are really attributable to other causes.

(ii) *Presence or absence of trypanosomes.*—This is valueless, since trypanosomes were only found in four instances (two in gland juice, one in blood, and one in C.S.F.) in 1,732 cases re-examined subsequent to treatment, and the true incidence of treatment-failures is certainly higher than suggested by these figures.

(iii) *C.S.F. picture.*—This is considered the only reliable criterion of cure in survivors, though it may perhaps be complicated by the co-existence of yaws in a community, since this disease apparently may rarely give rise to slight abnormality of the cerebrospinal fluid [this *Bulletin*, 1936, v. 33, 963 ; 1940, v. 37, 25 ; 1942, v. 39, 460]. However, yaws probably invalidates the criterion only to a very slight extent ; in 20 random individuals who had no history of sleeping sickness, and an unknown history in regard to yaws (which affects considerably more than half the population of this district at some time of their lives, generally in early childhood), Harding found that 19 showed 5 cells or less, and one showed 6·7 cells per cmm. of C.S.F.

A cell-count was considered to be a more sensitive index of the results of treatment than a total protein estimation. Thus, in 917 fluids examined for cells and protein, at the final survey, 71 were abnormal in that they showed cells above 10, or protein above 35 mgm., or both these features, but only 7 of the cases showed protein above 35 mgm. combined with a cell-count of 10 or less. The omission of protein estimation would, therefore, have entailed an error of about 10 per cent. in recording abnormal fluids, but in calculating total numbers of cases in which treatment failed, including those patients who died or became blind, the error would be no more than about 2 per cent.

In a minority of cases the cell-count was found to remain slightly raised up to three or four years after treatment even though there seemed every indication that the patient was cured. For this reason the author adopts 10 cells per cmm. as the limit of normality in assessing the cure-rate, but in order to satisfy the most stringent standards he has also worked out cure-rates on the basis that five cells per cmm. represents the upper limit of normality after cure. A definite decision as to cure cannot be reached within about 15 months after treatment.

(iv) *Mortality.*—A history of death from sleeping sickness is, of course, of prime significance in assessing the results of treatment, so long as the accounts of relatives and friends can be relied upon, as was found generally to be the case among the people concerned.

The author treats his findings by statistical methods designed to show the comparative value of the various forms of drug-therapy, in the mass treatment of a sleeping sickness outbreak which exhibits the distribution of evolutionary stages of the disease (as revealed by C.S.F. cell-counts) encountered in this particular epidemic. The distribution, as percentages of all cases of sleeping-sickness in which lumbar puncture was done before treatment, was as follows : 0–5 cells per cmm., 52·2 per cent ; 6–20 cells, 26·1 per cent ; 21–100 cells, 9·1 per cent. ; more than 100 cells, 12·5 per cent. The statistical methods used are fully described, and are similar in principle to those generally employed in calculating standardized death-rates from crude death-rates.

Course iii, comprising three doses of antrypol followed by three to five doses of tryparsamide, all at 5-day intervals, proved to be highly toxic, being followed by a standardized death-rate of 6·4 per cent. within three months of treatment. However, the toxicity- and death-rates associated with this course were considerably reduced by the adoption of course iv, where there was an interval of five to seven weeks after the first dose of antrypol, or where only one or two doses of antrypol preceded the administration of tryparsamide. In fact this course (iv) proved to be the most successful of all, with a standardized cure-rate of 93·5 per cent. Attempts to determine the underlying reasons for the exceptional toxicity of Course iii were unsuccessful, and the author considers that the most likely explanation of the great reduction in toxicity when the course was modified by merely allowing an interval of five to seven weeks between the first two antrypol doses, is that the long interval allowed time for recovery in the patients' general condition after the initial dose had destroyed all trypanosomes in the peripheral circulation.

Course ii (tryparsamide alone) was rated inferior to course iv largely because of the high incidence of blindness—5·6 per cent., though the figure is somewhat weighted by the high proportion of late cases treated, and vision is more frequently impaired in these than in early cases. Courses v and vi (diamidines) were inferior because of their failure to cure late cases.

A satisfactory rule for all occasions was eventually worked out : " if it is convenient to arrange an interval of 3 weeks or more without treatment after the first dose of antrypol has been injected, then a further two of antrypol followed by five of tryparsamide are given ; if the interval is between 2 and 3 weeks, only one further antrypol and six tryparsamide are given ; and if the interval is less than 2 weeks, then no further antrypol is administered and the course is completed with seven doses of tryparsamide. This rule has since been applied over many thousands of cases, and it has been consistently found that no more than about 1 per cent. of patients die during treatment and no more than 1 per cent. become blind."

An important part of the paper deals with the value of combined treatment by antrypol or pentamidine and tryparsamide. The author writes that it is generally less upsetting to the African peasant's farm work and normal life to visit a treatment centre once every 5 or 7 days than to visit it daily for the same number of times ; whereas such a patient would not be willing to make a journey of more than 3 or 4 miles daily for perhaps 10 days, he will and does walk four times that distance regularly once in 5 days on ten occasions. Greater practical advantage would therefore accrue from reducing the number of attendances necessary in the spaced type of course while retaining its effectiveness, than from reducing the intervals between injections. Such an aim might be realized by employing a combination of tryparsamide with another drug such that the two compounds could be administered concurrently in full doses without undue toxicity. Antrypol as the second drug does not meet the need because, when given concurrently with tryparsamide, the dose of one or both drugs must be substantially reduced for the combination to be

tolerated. Pentamidine, however, was safely given in full doses of 100 mgm. combined with five full doses (2 gm.) of tryparsamide, both drugs being given on each of five injection days at 5-day intervals, so that the whole course was completed in the short span of 3 weeks. The small-scale trials of combined pentamidine and tryparsamide (Courses vii to ix), involving 84 cases, appeared to give very promising results, but it was not possible to claim any superiority of the combination over tryparsamide alone, since the average Sierra Leone patient is so readily cured by tryparsamide without any adjuvant. The risk of toxic sequelae and visual impairment with the pentamidine-tryparsamide combination appears to be very slight, and the author recommends it for more extended trial in other parts of West Africa, where the average case is less responsive to treatment with tryparsamide.

The author has also studied the protection against subsequent reinfection, conferred by treatment. In 1,732 cases, comprising 1,610 probable cures and 122 relapses, re-examined at the final follow-up, trypanosomes were found in only four cases, although at least 41 reinfections might have been expected among the cured cases, on the basis of the prevailing infection-rate of the general population in the interim between mass-treatment and follow-up. Of these four cases, three had been treated by tryparsamide alone and probably were in fact reinfected individuals, because they had large soft glands suggestive of recent infection, and an almost normal C.S.F. picture. The fourth patient, who had received antrypol, was probably suffering a relapse, being clinically far advanced and with a high C.S.F. cell-count. In summary then, no reinfections were demonstrated in 1,307 cases treated by courses containing antrypol or a diamidine, though 33 might have been expected, whilst three reinfections occurred among 303 cases treated by tryparsamide alone, when eight might have been expected. The tentative interpretation offered is that all the treatment-courses produced a temporary immunity due to the destruction of trypanosomes, while antrypol and the diamidines (but not tryparsamide) exerted in addition a prophylactic action persisting for over a year. Harding writes that these findings are not necessarily representative of results which would be obtained in all parts of West Africa, and much depends, no doubt, on the local strain of trypanosome. In one small area in Nigeria, for example, he found trypanosomes in a large proportion of cases of relapse after treatment by tryparsamide alone, but in general his experience has been that trypanosomes are rarely to be found in relapses after combinations containing antrypol. Nevertheless, in another part of Sierra Leone, where an unusual type of the disease prevails, about 9 per cent. of a group of cases revealed trypanosomes 18 months after treatment with a combination of antrypol and tryparsamide, but whether they represented relapses or reinfections was not determined. Taking all such variations into account, the author's view is that it probably remains true that, in most types of West African trypanosomiasis, the inclusion of antrypol, or of a diamidine, in treatment courses reduces the danger to the community arising from the possibility of subsequent infectious relapse or reinfection among the cases treated. *E. M. Lourie.*

Dias, E. & de Freitas, L., Jr. Introdução ao estudo biométrico dos hemoflagelados do gênero *Schizotrypanum*. I. Introdução, material e técnica, problema e métodos estatisticos. [**Introduction to a Biometrical Study of Haemoflagellates of the Genus *Schizotrypanum*. I. Introduction, Material and Technique, the Problem and Statistical Methods.**] *Mem. Inst. Oswaldo Cruz.* 1943, June, v. 38, No. 3, 427–36, 1 fig. [14 refs.]

This is the first instalment of a series of papers devoted to a biometrical study of *Trypanosoma cruzi*-like haemoflagellates which the authors refer to

the genus *Schizotrypanum*. This group comprises trypanosomes parasitic in various species of mammals, and especially bats, in different parts of the world. Since these trypanosomes are morphologically similar to the parasite of Chagas's disease, it is important, both from the aetiological and epidemiological points of view, to determine whether they represent one species or a number of distinct species.

In the present paper the authors describe the methods employed for the differentiation of various strains of trypanosomes measured in blood-films stained by one of the Romanowsky methods. In each strain 50 trypanosomes are drawn with the aid of a camera lucida at a magnification of 1,500. The measurements are then made with an opisometer along a line running through the middle of the body of the trypanosome from the posterior end to the tip of the flagellum. They comprise the following elements: (1) Distance from posterior end to middle of the nucleus (PN), (2) distance from middle of the nucleus to anterior end of the body (NA), (3) length of free flagellum (Fl), (4) total length (T), (5) nuclear index (IN) representing PN/NA.

The statistical problem was to determine whether the strains thus measured belonged to the same or to different "populations". The authors consider that from this point of view the most important elements are NA and the "mean nuclear index" (INM), which is the mean of the individual nuclear indices (IN) of a strain. The strains are compared with each other by calculating the arithmetic mean of each series of measurements and the standard errors of the differences between the means, and also by applying Pearson's $\chi^2$ test.

*C. A. Hoare.*

Dias, E. & Torrealba, J. F. Verificação de flagelados semelhantes ao *Trypanosoma rangeli* Tejera, em *Rhodnius prolixus* alimentados em caso de doença de Chagas na Venezuela. Considerações sôbre a natureza dêste protozoário. [**Flagellates similar to *Trypanosoma rangeli* in *Rhodnius prolixus* fed on a Case of Chagas's Disease in Venezuela. Discussion of the Nature of this Protozoon.**] *Mem. Inst. Oswaldo Cruz.* 1943, Dec., v. 39, No. 3, 265–78, 35 figs. on 2 pls. [12 refs.] English summary.

In 1920 Tejera [see this *Bulletin*, 1921, v. 17, 97] described under the name *Trypanosoma* (or *Crithidia*) *rangeli* a flagellate, represented chiefly by crithidial forms, which he found in the gut of *Rhodnius prolixus* from Venezuela. In some of the bugs this parasite occurred alone, in others it was accompanied by metacyclic forms of *T. cruzi*. Tejera suggested that this parasite might also have some vertebrate host.

In the present paper the authors claim to have isolated *T. rangeli* from man. The case in question was in a child in Venezuela, who showed symptoms of acute Chagas's disease. The patient's blood was inoculated into a guineapig, and laboratory-bred *Rhodnius prolixus* were fed on the patient for xenodiagnostic purposes. The bugs thus fed became infected with flagellates which comprised crithidial forms similar to *T. rangeli* and metacyclic trypanosomes, while in the blood of the guineapig were found trypanosomes of the genus *Schizotrypanum*, to which the authors refer *T. cruzi* and some closely related bat-trypanosomes. The trypanosome in question was differentiated from *T. cruzi* biometrically, its closest affinities being with *T. phyllostomae*, a bat-trypanosome previously suspected of being capable of infecting man. The same trypanosome was also seen in a monkey inoculated from infected bugs and in guineapigs through which the strain had been passaged. However, the flagellates which developed in Triatomid bugs fed on these animals did not belong to the *rangeli*-type but were of the *cruzi*-type.

In discussing the nature of the new trypanosome, the authors dismiss both the possibility of a mixed infection (*T. cruzi* and *T. rangeli*) in the bugs, since these insects had been bred in the laboratory, and the possibility of it being an atypical strain of *T. cruzi*. They attribute all the stages seen in the bugs and in the mammals to *T. rangeli*, which they regard as a pathogenic human trypanosome.

[There are a number of conflicting facts in this paper which stand in need of further elucidation before the authors' conclusions can be accepted: (1) It is admitted that the symptoms in the patient from whom "*T. rangeli*" was isolated were those of typical Chagas's disease, as produced by *T. cruzi*. (2) The blood-form of "*T. rangeli*" has the general appearance of *T. cruzi* from which it differs only in its "mean nuclear index" (see DIAS & FREITAS, above) and "mean total length." In other words, there is evidently considerable overlapping in the dimensions of the two trypanosomes, which would hardly justify their separation into distinct species, especially as no information is given regarding the degree of variation in undoubted strains of *T. cruzi*. (3) It would appear that while the crithidia in the bugs infected from the patient correspond to Tejera's *T. rangeli* in having a *small* kinetoplast, both the blood-form of the new trypanosome and its metacyclic form in the bug have a *large* kinetoplast, like that in *T. cruzi*. Since the kinetoplast of a given trypanosome retains its characteristic size throughout the entire cycle of development in vertebrate and invertebrate hosts, the discrepancy found in the present case (but not commented upon by the authors themselves) is rather suggestive of a mixed infection of *T. cruzi* and Tejera's flagellate. (4) The problem is further complicated by the fact that *rangeli*-like crithidia developed only in the bugs which had fed on the patient, but not in those which were subsequently fed on experimentally infected animals.] *C. A. Hoare.*

ROMAÑA, C. & TERRACINI, E. Infección de lauchas por *S. cruzi* à través de la piel intacta. [**Infection of Mice *via* the Intact Skin.**] *An. Inst. de Med. Regional.* Tucumán. 1945, Aug., v. 1, No. 2, 135–40. [10 refs.] English summary.

"(*a*) The authors have obtained with *S. cruzi* the infection of mice through the apparently intact skin.

"(*b*) The *prepatent period* lasted 73 days in the infected animals.

"(*c*) The infection showed a chronic character from the beginning."

ROMAÑA, C. & TERRACINI, E. Comportamiento de las infecciones de lauchas por *S. cruzi*, segun la concentración de parasitos inoculados. (Infecciones crónicas iniciales.) [**The Course of Infections of Mice with *T. cruzi*, according to the Number of Parasites Injected.**] *An. Inst. de Med. Regional.* Tucumán. 1945, Aug., v. 1, No. 2, 141–64, 5 graphs. English summary.

LARCHER, M. & ROMAÑA, C. La puerta de entrada cutanea en los casos humanos de enfermedad de Chagas. [**The Portal of Entry in Human Cases of Chagas's Disease.**] *An. Inst. de Med. Regional.* Tucumán. 1945, Aug., v. 1, No. 2, 165–75, 3 figs. [12 refs.] English summary.

The local swelling associated with the bite of the vector of *T. cruzi* has often been described, but the authors here give a detailed account of the lesion. It is red, oedematous, hard and slightly painful on palpation. The associated glands, preauricular and submaxillary, are tender and, if sections of the former are examined, developmental forms of *T. cruzi* are seen, and soon general symptoms appear and trypanosomes are present in the blood. In some cases

the site of the bite is like a furuncle or an anthrax pustule of mild intensity ; in others there is superficial rather than deep extension and an erysipelatoid condition is produced. It then gradually clears up, the skin becomes dry and undergoes a furfuraceous desquamation, leaving a small nodule or a pigmented spot.

A case in point is detailed : A man of 27 years ; the primary lesion was at first thought to be pyogenic and he was treated with sulphonamides, but without benefit. He also had a rose rash on the chest and shoulder, slightly raised, disappearing on pressure. The primary lesion of the eyelids and face were erysipelatoid next day and then began to clear up. A fortnight after admission the patient complained of pain in the bones, especially the long bones. Complement fixation was now weakly positive. In another fortnight the reaction was definitely positive and after another 14 days strongly so. The local lesion gradually disappeared and two months after admission to hospital the only indication of it was a slight pigmentation of the skin.

*H. Harold Scott.*

ROMAÑA, C. Parasitismo por *S. cruzi* de válvulas de corazón de perro. [**Infection of the Cardiac Valves of the Dog with** *T. cruzi*.] *An. Inst. de Med. Regional.* Tucumán. 1945, Aug., v. 1, No. 2, 207–11, 2 figs. English summary.

" The author refers to the finding, in the atrio-ventricular valves of a dog's heart, of focus of multiplication of *S. cruzi*, describing the local histopathological reaction produced by the parasite."

ENGEL, R. Tumorwachstum und Chagaskrankheit. [**New Growths and Chagas's Disease.**] *Klin. Woch.* 1944, Mar./Apr., v. 23, Nos. 9/16, 127–9, 3 charts. [11 refs.]

ROSKIN and ROMANOWA have reported the cure of experimental cancer by means of the toxin of *T. cruzi*, but, says the author, the story of the treatment of cancer is loaded with uncritical communications and defective experiment. Next, Rudolf SCHMIDT, as long ago as 1910, decided that he was convinced by statistical figures that those who had recovered from several infective diseases were less liable to malignant disease than those with a " low infective index."

ROSKIN and ROMANOWA (*Acta Cancrol.*, 1935, v. 1, 323) noted that in Chagas's disease, after the acute stage subsides, the trypanosomes disappear from the blood and collect, in leishmania form, in the heart, brain and internal organs and, when present, in tumour cells. Next, if tumour emulsion and *T. cruzi* are inoculated together, the latter infection gains the ascendency, the tumour dwindles and may even disappear altogether. They went a step further and prepared a toxin of the trypanosome from centrifuged citrated blood, cooling it and again heating to destroy the trypanosomes themselves, and they claimed that increasing doses of this endotoxin-containing material first retarded and then prevented the growth of the tumour without harming other tissues or organs.

The author has carried out experiments with large numbers of mice, which are very susceptible to *T. cruzi* infection, the tumour being one to which mice are liable (mouse-ascites tumour). These experiments were carefully performed, but the author was unable to confirm the work or report of Roskin and Romanowa. The toxin in the acute stage had no beneficial effect on the tumour growth and the tumour was absolutely unaffected in its course by Chagas's disease in its chronic stage or after cure. So much for the mouse tumour ; the application to cancer in human beings has not yet been tested [but one gathers from the general tone of the paper that success would come as a surprise].

*H. Harold Scott.*

TALICE, R. V. & LÓPEZ-FERNÁNDEZ, J. Primeros ensayos de tratamiento de las formas agudas de enfermedad de Chagas con un nuevo arsenical (ácido p. arsenofenilbutírico). [**Trial of a New Arsenical in the Treatment of Acute Chagas's Disease.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1945, July, v. 27, No. 1, 33–46, 3 charts. English summary.

The best treatment hitherto known for acute cases of Chagas's disease has been Ac. 7602, a German preparation which of late has not been obtainable. The preparation here referred to is *p*-arsenophenyl butyric acid, with the formula

It has been found of service a year ago for African trypanosomiasis by EAGLE, the protozoon disappearing from the blood within an hour of the first injection.

For cases of American trypanosomiasis it has been used in a 2 per cent. solution in distilled water, injected intravenously or intramuscularly three times a week in doses of 0·015 cc. per kilo body weight, till 12 doses have been given. Three cases are recorded in this paper : two children, of 5 and 12 years respectively, and an adult of 26 years. All three were clinically typical cases. The children tolerated the drug well ; the adult had albuminuria after the second injection, which necessitated reduction of the dose and longer spacing between injections [but no details are given of this reduction or lengthening of interval]. The results noted are not too optimistic ; the fever dropped in four days, but other symptoms persisted, though the regional adenopathy was reduced. Xenodiagnosis, positive before treatment was started, became negative after four days, but in the two children was again positive when they left hospital after the 12th injection. In untreated cases, even when the form of disease is mild, the trypanosomes persist for a month at least. The clinical evolution of the disease seems to be uninfluenced. The fact that in the children the xenodiagnosis was negative for short periods only, 7 and 12 days respectively, while it remained so in the adult, leads to the observation that larger doses should be given to children suffering from this disease.

*H. Harold Scott.*

TALICE, R. V. Ensayo de tratamiento de la forma aguda de la enfermedad de Chagas por la penicilina. [**Treatment of Acute Chagas's Disease with Penicillin.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1945, Aug., v. 27, No. 2, 152–7, 1 chart & 4 figs. English summary.

" One acute case of Chagas disease, in a 11 years boy, has been treated with penicillin, intravenously. The total doses reached to one million Oxford units which were distributed through 12 days of treatment.

" The treatment had no beneficial action either from a clinical or a parasitological standpoint. The patient left the hospital still with a mild, slight fever and 12 xenodiagnoses carried on every day, were all positive.

" Although only one case has been treated, we think that penicillin has no action over *Trypanosoma cruzi* infections. This result confirms our own experiments on laboratory animals."

PÉREZ, A. & ROMAÑA, C. Estado actual de antiguos casos de enfermedad de Chagas en una familia de Monteros (Tucumán). [**The Present Condition of Patients with Long-standing Chagas's Disease in a Family.**] *An. Inst. de Med. Regional.* Tucumán. 1945, Aug., v. 1, No. 2, 213–28, 6 figs. English summary.

" Within the same family, the authors establish the existence of :—

" (*a*) An old acute case of Chagas disease, the first described in Argentina, 20 years ago, now seemingly a simple *carrier* of *S. cruzi*.

"(*b*) An old case of Chagas disease with an apparent *spontaneous cure*, examined 15 years afterwards. The isolated strains, in both cases, during the acute period, showed little virulence.

"(*c*) Finally, the father had a miocardiac lesion, probably caused by Chagas disease."

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## LEISHMANIASIS.

Gast Galvis, A. & Rengifo, S. Leishmaniosis visceral. Estudio epidemiológico del primer caso diagnosticado en Colombia. [**First Case of Kala Azar diagnosed in Colombia.**] Reprinted from *An. Soc. Biol. Bogotá.* 1944, Sept., v. 1, No. 4, 8 pp., 3 figs.

During the course of a viscerotomy survey being carried out in Colombia in order to identify deaths from yellow fever, sections of the liver from a child three years of age were found to contain numerous leishmania. The case was evidently one of kala azar, the first to be identified in this country. A careful study of the inhabitants of the district, San Vicente de Chucuri, Department of Santander, failed to reveal any other case. There was a 9·33 per cent. incidence of malaria, a fact which renders difficult the recognition of cases of kala azar. During the survey which was carried out a number of cases of cutaneous leishmaniasis were seen. A study of the arthropods of the district showed that 15 species of *Phlebotomus* were represented. *C. M. Wenyon.*

da Cunha, A. M. A soro-aglutinação das leishmanias. [**Serum Agglutination of the Leishmanias.**] *Mem. Inst. Oswaldo Cruz.* 1942, v. 37, No. 1, 35–76. English summary.

The author has investigated the possibility of identifying species of *Leishmania* by agglutination tests carried out with sera prepared by immunizing rabbits with culture forms of the organisms. The species employed were *L. tropica*, *L. infantum* and *L. donovani* of the Eastern Hemisphere and *L. brasiliensis* and *L. chagasi* (*L. donovani*) of the Western Hemisphere. A number of different strains of each species, some of which had been in cultivation for years, and others recently isolated, were used. Agglutination tests and absorption tests were carried out. The general results are given in a series of tables. It is concluded that all strains, when freshly isolated, have the same antigenic constitution. It was noted that when a serum which had been prepared against a freshly isolated strain is absorbed with an old strain, the amount of agglutinin left free is much smaller than when a serum prepared against an old strain is absorbed with a newly isolated strain. It was shown that, by absorbing equal amounts of serum prepared against a new strain, by equal amounts by weight of a new and an old strain, a newly isolated strain absorbs a larger amount of agglutinin than does an old strain. The absorbed sera were made to act on recently isolated as well as on old strains, with the object of deciding whether the newly isolated strains contained a greater amount of the common antigen or whether they possessed a Vi antigen. The result indicated that the former view was correct. The antigen in newly isolated cultures is a common or primitive antigen which, with increasing age of the culture, is subject to modifications due to the production of secondary antigens which are not species-specific. The final conclusion is that species of *Leishmania* cannot be identified by serological agglutination tests. [Though this final conclusion may be correct, as also the assumption that freshly isolated strains of all species contain a common antigen, it is not clear that the recently

isolated strains contain no other antigen, for the author has not applied the methods now generally employed for the antigenic analysis of bacteria and viruses, *e.g.* exposure to the action of heat and various chemicals. The application of such tests might show that the results are capable of a different interpretation.] *C. M. Wenyon.*

SWEENEY, J. S., FRIEDLANDER, R. D. & QUEEN, F. B. **Kala-Azar (Visceral Leishmaniasis) simulating Splenic Anemia.** *J. Amer. Med. Ass.* 1945, Aug. 4, v. 128, No. 14, 1020–22, 3 figs.

The case described is that of an Italian enlisted man, 22 years of age, who was admitted to hospital in Utah, U.S.A., for an acute surgical condition of the abdomen. There had been a two-years' history of illness which had commenced in Sicily. Numerous examinations failed to reveal the cause of the splenic enlargement and marked leucopenia which were features of the case. Finally the case was considered to be one of splenic anaemia. The spleen was removed, and a correct diagnosis was established by the discovery of leishmania in sections of the organ. Many previous examinations of preparations of the blood and bone marrow had failed to reveal the parasite. The patient was given a course of neostibosan and made an uneventful recovery.

*C. M. Wenyon.*

ADLER, S., TCHERNOMORETZ, I. & BER, M. **The Action of some Aromatic Diamidines on Cultures of** *Leishmania donovani*. *Ann. Trop. Med. & Parasit.* 1945, May 31, v. 39, No. 1, 14–19.

The authors have tested a series of aromatic diamidines on cultures of *Leishmania donovani* with the object of correlating the results, if possible, with those obtained in the treatment of experimentally infected hamsters as previously reported [this *Bulletin*, 1940, v. 37, 775; and 1942, v. 39, 748]. It was found that in the highest concentration of each drug which still permits survival and retention of motility of flagellates there is a definite inhibition and even abolition of the capacity to multiply. For each compound there is a fairly well defined maximum concentration which permits 90 to 100 per cent. of normal growth. There is no sharp end-point at which all the flagellates disappear. The two most effective drugs tested were 4 : 4′-diamidino diphenoxy propane [propamidine] and 4 : 4′-diamidino diphenoxy pentane [pentamidine], both of which have been shown to be inferior to 4 : 4′-diamidino stilbene [stilbamidine] in tests on hamsters. There is thus no correlation between the results of *in vitro* and *in vivo* tests, though the four least effective compounds were in this position in both tests. *C. M. Wenyon.*

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## FEVERS OF THE TYPHUS GROUP.

SYLLA, A. Fleckfieberbeobachtungen. [**Observations on Typhus Fever.**] *Deut. Militärarzt.* 1944, June, v. 9, No. 6, 263–72.

A clear and detailed description is given of the clinical features of typhus fever as observed by the author during the recent war. Numerous references are also made to papers already reviewed in this *Bulletin*.

Some points from the paper are as follows: (the figures in brackets show the percentage incidence and when two figures are enclosed in one pair of brackets the first shows the incidence in cases with recovery, the second refers to fatal cases),

The disease, on the whole, was mild ; the average fatality rate was about 6–7 per cent. but there was a wide range of variation in different groups of cases ; the extremes ranged from 1 to 15 per cent. Even during the same outbreak there might be great differences in severity at various stages of the epidemic. The incubation period ranged from 8 to 21 days. During the first three days the temperature fell to normal in some cases for a few hours, then rose to about 39°C. and persisted at that level. The fever curve was usually of the continued type (89·3), but in some cases was remittent or intermittent. A pseudo-crisis occurred in 12 per cent. of the cases about the 10th day. The termination was by lysis (70) or crisis (30) : an " after-fever " occurred in many cases (25·6).

The rash might be pale and scanty (50), dark red (38·7), or of irregular types such as papular, scarlatiniform, morbilliform, etc. (4·5) ; petechiae were often seen (23 and 55). Pulmonary manifestations were : bronchitis (50 and 65) ; bronchopneumonia (7 and 25·8) ; and lobar pneumonia (1·3 and 11). Cardio-vascular failure was attributed to myocarditis (10 and 49·7) or peripheral circulatory disturbance (13·8 and 86·5). Venous thrombosis was not common (1·6 and 3·7) ; gangrene was rare ; amputation of a limb was needed in only one case. Arterial spasm (1·3) rather than arterial thrombosis occurred in a few cases in the limbs.

The nervous manifestations were : delirium (24·8 and 73·6) ; various psychoses especially mania and suicidal tendencies (6·3 and 34·9) ; tonic-clonic spasms (1·1 and 24·8) ; nerve pareses (0·8 and 9·2) ; hardness of hearing (26), sometimes associated with inflammation of the middle ear (3·8).

Diagnostic importance was attached to the prolongation of the latent period of dermographism.

Diarrhoea (17), enlargement of the liver (5), icterus (1·1), and enlargement of the spleen (58) were observed in the stated percentages. Slight albuminuria was usual, the urine often contained red and white blood cells and cylindrical casts ; a true nephritis occurred in 10·8 per cent. of the cases.

The blood picture was very varied ; leucocytosis occurred in about half of the cases, leucopenia was not infrequent. The leucocytic index always showed a shift to the left. Septic complications were few.

The chief findings at autopsies were myocarditis, slight (39·2) or severe (33), pneumonic complications (47), swelling of the kidneys (100), splenic enlargement (98), and oedema of the brain (100). No enthusiasm is shown for some of the special treatments that have been vaunted by some other German observers ; warm baths, sulphonamides, and atebrin were regarded as of doubtful value. Strophanthin, caffeine, and adrenaline were found useful ; glucose transfusions, sometimes in concentrated form, were occasionally needed. The general treatment was on orthodox lines. *John W. D. Megaw.*

Claus, G. Über Mittelohr- und Warzenfortsatzentzündung bei Fleckfieber. [**Middle-Ear and Mastoid Inflammation in Typhus Fever.**] *Deut. Militärarzt.* 1944, Aug., v. 9, No. 8, 366–70, 2 figs. [12 refs.]

Four cases are described in which pyogenic complication affected the middle ear with extension to the mastoid process. Although the condition is not common it is not so rare as is generally supposed, and it deserves attention because of the danger of extension to the lateral sinus. Two exceptionally clear X-ray photographs illustrate the paper, and a description is given of the operative technique. *John W. D. Megaw.*

Rigler, R. Physiologisch-chemische Untersuchungen bei Fleckfieberkranken. [**Biochemical Investigations in Typhus.**] *Deut. Militärarzt.* 1944, Aug., v. 9, No. 8, 377–80, 1 fig.

An investigation of the non-protein nitrogen, sugar, and chloride concentrations of the blood and blood serum in typhus fever.

Richet, C. Notes sur le typhus exanthématique observé à Buchenwald. [**Typhus in the Buchenwald Concentration Camp.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1945, Nos. 15/16, 183–7.

Ecke, W. Proteus-OX19-Agglutination und Rickettsien-Agglutination bei Fleckfieberschutzgeimpften. [*Proteus OX19* **and Rickettsia-Agglutination Reactions in Persons Protected by Typhus Vaccines.**] *Deut. Militärarzt.* 1944, Apr., v. 9, No. 4, 188–91. [10 refs.]

The titres observed in groups of persons vaccinated (presumably recently except in the group vaccinated 4–6 months previously) with Weigl's louse vaccine or a Cox-type vaccine, were as shown in the table. With regard to the first group of 130 it is stated that 109 had received Weigl's vaccine and 21 the Cox-type vaccine ; positive reactions were relatively much more numerous in the latter sub-group, but no details are given.

*Weil-Felix Titres.*

| | Negative | 1–50 | 1–100 | 1–200 | 1–400 |
|---|---|---|---|---|---|
| Among 130 vaccinated ... | 51 | 31 | 31 | 15 | 2 |
| Among 49 vaccinated 4–6 months previously ... | 34 | 7 | 4 | 4 | 0 |

*Rickettsia-Agglutination Titres.*

| | Neg. | 1–20 | 1–40 | 1–80 | 1–160 | 1–320 | 1–640 | 1–1,280 |
|---|---|---|---|---|---|---|---|---|
| Among 100 vaccinated ... ... | 2 | 3 | 9 | 41 | 19 | 13 | 12 | 1 |

*John W. D. Megaw.*

Shoukri, Y. S. **Bedside Typhus Diagnosis.** *J. Roy. Egyptian Med. Ass.* 1945, May, v. 28, No. 5, 231–45.

The introductory " blurb " states that the method described is " A quick and simple variation of the Weil-Felix reaction, giving positive results much earlier than the original test in 50 per cent. of the cases."

The test is a slight variant of a well-known slide test. A droplet of finger blood is mixed with a drop of plain water ; a drop of a thick suspension of *Proteus OX19* stained with methylene blue is added and stirred in for 30–90 seconds. The method of preparing the suspension is described. The growth from 10 agar 20-hours' slope cultures is mixed with 10 cc. distilled water, and two drops of formalin are added. After filtering the suspension through a thin layer of cotton, 0·2 cc. German Loeffler's blue solution is added ; the mixture is well shaken and kept in the incubator for a day or two, being shaken twice daily during the process ; it is again filtered through cotton and another drop of formalin is added.

The degree of dilution of the blood on the slide is 1–7.

It is claimed that the use of water and formalin abolishes the " agglutination inhibitory zone " of the serum, that the water prevents coagulation and haemolyses the red corpuscles, and that false positives due to natural agglutinins do not occur.

From the table showing the results of comparative tests it appears that all titres below 1–125 with the standard Weil-Felix test are shown as negative results. This arbitrary elimination of weak positives must be taken into account in estimating the significance of the findings. *John W. D. Megaw.*

LORENTZ, F. H. Der Trockenfolientest zur raschen Erkennung des Fleckfiebers. [**The Dry-Leaf Test for the Rapid Diagnosis of Typhus Fever.**] *Med. Ztschr.* 1945, Jan., v. 1, No. 4, 128–30, 6 figs.

The author describes the results obtained in a large series of tests carried out by the method introduced by EYER and BRIX [see this *Bulletin*, 1944, v. 41, 23]. The only special requisite for the test is a supply of ready-prepared slips of paper, on each of which a drop of stained suspension of *Proteus OX19* has been dried, but details of the technique will be of interest only to workers engaged in testing the various rapid modifications of the Weil-Felix reaction.

From the present paper it is evident that the method demands a good deal of practice ; the first series of 100 tests yielded a number of anomalous results and so have been discarded from the final analysis, which deals with a series of 1,000 consecutive tests and compares the findings with those obtained by means of the standard reaction.

A general degree of agreement is claimed between the two tests, and broadly speaking the relationship between the reactions was as follows : Negative reactions correspond to negative Weil-Felix responses ; weakly positive reactions (±) correspond to titres of about 1–200 ; positive reactions (+) to titres of about 1–600 ; and the two highest grades of reaction (++ and +++) to titres of 1–3,000 and over.

The table shows that there was a good deal of variation from this standard ; for example among 106 negative reactions with the rapid test there were 52 in which the Weil-Felix titre was ± 1–100 or +1–100.

Among 378 weakly-positive reactions, the Weil-Felix titres were ±1–100 in 73, +1–100 in 57, +1–200 in 176, +1–400 in 61, +1–800 in 9, +1–1600 in 2. *John W. D. Megaw.*

CLAVERO, G. & GALLARDO, F. P. **Giroud's Intradermic Test in Typhus Fever Infection. Personal Observations, Techniques, and possible Applications.** *Bull. Health Organisation* (League of Nations). 1943/44, v. 10, No. 4, 700–21, 8 figs. on 4 pls. [30 refs.]

The original article was reviewed in this *Bulletin*, 1943, v. 40, 530.

SCHMIDT, W. Erfahrungen zur Therapie des Fleckfiebers. [**Experiences in the Therapy of Typhus Fever.**] *Deut. Militärarzt.* 1944, June, v. 9, No. 6, 273–6, 1 fig.

The author claims to have saved a number of lives by injections of insulin—which in severe cases was given up to the point of causing hypoglycaemia—followed by the administration of glucose, preferably by the mouth, but intravenously when necessary. The dosage of insulin when possible was based on blood-sugar estimates during the fasting period. Comatose patients were given up to 20–30 gm. glucose intravenously every day.

The fatality rate in a group of patients treated by insulin and glucose when necessary was 6·3 per cent. ; in another group, stated to be comparable in all other respects, the rate was 11·9 per cent., but no information is given with regard to the size of the two groups or the other circumstances which justified a statistical comparison of the results. *John W. D. Megaw.*

SCHÖNBRUNNER, E. Strophanthin und Digitalistherapie bei Fleckfieber. [**Strophanthin and Digitalis Therapy in Typhus Fever.**] *Deut. Militärarzt.* 1944, Sept., v. 9, No. 9, 412–15, 4 figs. [27 refs.]

Full details are given of an exceptionally severe case of typhus fever in which the pulse rate rose to 160 on the 14th day and continued to rise in spite of " strophanthin-glucose thrice daily." On the 16th day the rate was 170–180 and frequent doses of strophanthin were given intravenously, amounting in all to 1·25 mgm. The rate rapidly fell to 100 and there was a great improvement in the patient's condition.

The strophanthin-effect lasted a short time and in spite of further injections the rate rose as high as before. Digitalis was given in the form of 2 cc. " Digipurat " every six hours and the rate fell promptly to 100–140. By the 26th day the improvement was so great that the dose of digitalis was given only once daily.

The author states that there are practically no contraindications to the " strophanthin (digitalis) " treatment in typhus fever, whether the circulatory failure is due to myocarditis or to damage to the vasomotor centres.

In the case described the reductions in the pulse rate were due to the production of a 2–1 heart block, as is shown by the electrocardiograms.

*John W. D. Megaw.*

GRÜBEL, W. Ueber die Fleckfieber-Rekonvaleszenz mit besonderer Berücksichtigung des Kreislaufes. [**Convalescence in Typhus Fever with special reference to the Circulatory System.**] *Münch. Med. Woch.* 1944, Aug. 25, v. 91, Nos. 33/34, 426–9.

The author begins by referring to the expansion of the German " lebensraum " to the East as being responsible for a renewed interest in typhus fever.

The present study deals with 119 convalescent patients aged 19–43 years who were kept under observation till about three months after the onset of the illness. Careful records were kept of the results of simple tests of circulatory efficiency, and an analysis is given of the findings before and after exercise-tolerance tests carried out at various stages of convalescence. According to the criteria adopted by the author for estimating the significance of these tests it was found that four weeks after the onset of the illness 81·5 per cent. of the patients had a definite degree of circulatory insufficiency ; 15·1 per cent. had " circulatory lability," and 3·4 per cent. gave normal responses to the test. Twelve weeks after the onset the corresponding figures were 31·9 per cent., 51·3 per cent., and 16·8 per cent. Abnormal increases, after exercise, in the pulse and respiration rates and in the pulse pressure were regarded as reliable indications of circulatory disturbances.

Electrocardiographic examinations were made in 89 cases ; in 13 of these there was evidence of coronary insufficiency or myocardial damage, but at the end of four months only four patients showed any abnormality. Permanent myocardial damage was believed to be of rare occurrence. Among patients observed between the 4th and 12th weeks the lymphocyte count was increased in 68 per cent. and the eosinophile count in 46 per cent.

The blood-sedimentation rate remained high for a long time in most of the cases.

The complications observed among the patients studied were: acute glomerulonephritis in one patient, this occurred on the 7th day and recovery was complete by the end of seven weeks; slight joint rheumatism in two patients; urticaria in one; and angioneurotic oedema in one. These complications had no obvious effect on the circulatory system. *John W. D. Megaw.*

Nyka, W. **A Histological Study of the Lungs of Mice infected with Typhus Rickettsiae.** *J. Path. & Bact.* 1945, July, v. 57, No. 3, 317–24, 12 figs. on 4 pls.

The author describes the histology of the lungs of mice inoculated intranasally with murine or epidemic strains of typhus rickettsiae; three of the former and seven of the latter strains were used. The methods of preparing the infecting suspensions and of fixing and staining the lungs are described. The following improved method of staining was employed.

Fix lung sections in 10 per cent. neutral formol; stain in 1 : 10,000 aqueous methyl violet, ½–1 hour: differentiate in weak acetic acid (2 drops to 100 cc. water) until the cytoplasm is unstained; counterstain with 1 : 10,000 aqueous metanil yellow, a few seconds; acetone, xylol, mount in "Xam" (Gurr) or DPX4 mounting medium (Media Mounting Centre).

The paper is illustrated by 12 excellent photomicrographs. Large numbers of mice were employed. In those allowed to die of the disease there was complete consolidation of the lungs, often with a small amount of pleural exudate; in the mice that were sacrificed, various stages of congestion and consolidation were observed. In the congested areas all the blood vessels, especially the alveolar capillaries, were dilated, and the epithelial cells of the alveoli were swollen.

Consolidation was due either to inflammatory oedema or to swelling of the epithelium and packing of the lumen with desquamated alveolar cells and with leucocytes. In many places the vessels and bronchioles were seen to be surrounded by thick cuffs composed chiefly of monocytes.

The usual types of rickettsiae were seen; some were extracellular and occurred either in discrete form, in clumps, in large groups, or in masses, in the alveoli. Intracellular rickettsiae were most abundant in the alveolar cells, whose cytoplasm sometimes was completely packed with cocco-bacilliform or rod-shaped organisms; in other cells there were masses of granular forms. The endothelial cells of the vessels seldom contained rickettsiae; this finding is in sharp contrast with the special invasion of these cells described as occurring in guineapigs inoculated intraperitoneally.

Lungs infected by murine rickettsiae were on the average much richer in the organisms than those infected by epidemic strains; otherwise the changes caused by the two types of rickettsiae were similar.

Secondary infections were surprisingly rare, whether or not the mice had been treated by sulphonamides. It is suggested that the rickettsiae inhibit the growth of bacteria. *John W. D. Megaw.*

Philip, C. B. & Kohls, G. M. **Studies on Tsutsugamushi Disease (Scrub Typhus, Mite-borne Typhus) in New Guinea and Adjacent Islands. Tsutsugamushi Disease with High Endemicity on a Small South Sea Island.** *Amer. J. Hyg.* 1945, Sept., v. 42, No. 2, 195–203, 4 figs.

This study was carried out under the auspices of the U.S.A. Typhus Commission. The authors investigated an outbreak of tsutsugamushi disease which occurred on South Bat Island, situated about 60 miles south of the Admiralty Islands and having its total area of about 46 acres completely

covered by cocoanut palms under which sparse grass and scattered undergrowth grow. Normally the island is uninhabited except for periodic visits by natives for harvesting the cocoanuts.

The island swarms with rats—*Rattus concolor browni*—there were 15 pigs of the domestic type, which lived in wild conditions; fruit bats and several species of birds were also found.

The only biting insect that was detected was *Aëdes scutellaris*. Large numbers of larval mites were found on the rats; these were *Trombicula deliensis* Walch, 1923, which H. Womersley has now reported to the authors to be identical with *T. walchi* Womersley and Heaslip, 1943. *Schöngastia pusilla* Womersley, 1944 was abundant in boot collections but was not found on any of the animals or birds that were examined: it was probably responsible for scrub itch which occurred among the occupying troops. A few specimens of an apparently new species of *Neoschöngastia* were found on a bird, the ground-living rail, *Rallus philippensis*. No other species of mite was found.

Each of five pools of triturated *T. deliensis* from the rats was inoculated intraperitoneally into four white mice, and one very large pool of the same larval mites was inoculated into eight mice. Most of the mice died, either within the first two days, or later of intercurrent infection, so that by the end of 15 days only three mice survived, one from each of three pools. From each surviving mouse a virulent strain of *Rickettsia orientalis* was isolated; one strain which was transmitted through 29 mouse passages killed the animals on the average in 5½ days; it killed nine of ten inoculated guineapigs.

Among 41 white persons who camped on the island for varying periods between the end of February and the middle of April 1944, and who could be traced afterwards, there were 26 definite cases of tsutsugamushi disease. There were two deaths, and most of the patients were seriously ill.

A minority of the campers had slept in hammocks and escaped infection; the majority had slept on cots placed on wooden floors raised from the ground.

The incidence of some of the chief features of the disease is shown in a table. Among the 24 for whom reasonably complete information was available, the duration of the fever ranged from 12 to 23 days, except for one patient in whose case it lasted 8 days. An eschar was seen in 14 cases, in 8 it was not detected, and for the remaining two the information was doubtful. A rash was seen in 11 cases. The results of the Weil-Felix test (*Proteus OXK*) are given for 19 patients; in 6 it was negative, but the test was not made till the 35th to the 47th day: in the others the titre ranged from 1–80 to 1–160 or over; most of the tests were made after the 20th day.

This is the first time that *T. deliensis* has been found infected in natural conditions; the only other species hitherto found naturally infected are *T. akamushi* in Japan, and *T. fletcheri* in New Guinea.

The high degree of prevalence and virulence of the infection among mites in the island is regarded as being due to the great density of the rat population and the consequent opportunities that exist for rapidly recurring transmissions from rat to mite and from mite to rat. *John W. D. Megaw.*

Klein, H. S. **An Epidemic of Scrub Typhus.** *J. Roy. Army Med. Corps.* 1945, Oct., v. 85, No. 4, 187–90.

The author describes the clinical features of an outbreak of scrub typhus which occurred in the months of October, November and December 1944, in the Chin Hills of North Burma. Although 225 patients were admitted to hospital during the period the present description deals only with 41 cases among British soldiers; the other cases, among Indian troops, are said to have been essentially similar in type.

The incubation period ranged from 4 to 14 days; the onset was sudden in about two-thirds of the cases, in the others there were feverish headache and malaise for two or three days before the onset. In the early stages of the illness the disease closely resembled louse-borne typhus; by the third day the patients were seriously ill; extreme apprehension was a conspicuous feature, and it is stated that dread of the disease was universal among the British troops most of whom "preferred the Japs." This psychological factor [which has been emphasized by several observers in the Pacific area] was suspected of contributing to the high fatality rate among the British patients, of whom five (about 12 per cent.) died, whereas only seven deaths (3·8 per cent.) occurred among the 184 Indian patients.

An eschar was seen in 34 per cent. of the patients; generalized lymphadenitis occurred in all the cases, but lymphangitis was never seen. All but one of the patients had a rash of a dull red colour; it was macular in 30 cases, maculo-papular in seven, papular in two, and morbilliform in one. The rash appeared first on the trunk and soon extended to the arms, legs and face; the palms and soles were never affected.

In all but two of the patients who recovered the termination was by lysis. In four of the fatal cases there was a sudden drop in the temperature with collapse, followed by a terminal rise just before death, which occurred on the 13th, 14th, 15th and 21st days.

In four cases malaria parasites were found, these were benign tertian in three and malignant tertian in one.

The chief complications were as follows:—Bronchitis occurred in 32 cases, and pulmonary infarction in seven. The indications of infarction in four of these were, sudden pain in the chest, cough and haemoptysis; in three there were pain and cough without haemoptysis; and in one case, which was diagnosed after death, the only symptom was epigastric pain. Lobar pneumonia occurred in one case, in which it was the chief cause of death. Pharyngitis, with laryngitis and tonsillitis, was present in four cases. Half of the patients had temporary deafness; five had retention of urine; and five had severe mental symptoms—delusions, hallucinations, or delirium—but all made good recoveries. There was one case of femoral thrombosis, also with recovery.

The changes that were found after death in all the fatal cases were, oedema and congestion of the brain, "small pale, and toxic-looking heart," slight hypostatic congestion of the lungs, and enlargement of the intrathoracic lymph glands. There was mononuclear infiltration between the muscle fibres of the heart and "slight decrease in the adrenal cortex."

No benefit was observed from the use of penicillin; sulphonamides were administered to all patients who had chest complications; given also after catheterization, they were believed to have prevented secondary urinary infection.

A fluid intake of 8 to 10 pints was aimed at in spite of the cool situation of the hospital at a height of 5,000 feet. Twenty grains of sodium chloride were added to each pint of liquid. The diet included such articles as bread, biscuits, and tinned fruits; 2,400 calories were given daily. Lumbar puncture caused dramatic improvement in four semi-comatose patients whose cerebrospinal fluid pressure was high, but it failed in one case in which the pressure was low.

*John W. D. Megaw.*

ANDREW, R. **A Note on the Incubation Period of Scrub Typhus and its Correlation with Clinical Severity.** *Med. J. Australia.* 1945, Sept. 15, v. 2, No. 11, 335–6.

In a group of cases of scrub typhus in North Queensland it was possible to fix the incubation period with a considerable degree of reliability. Among 2?

cases, 10 were classed as being severe (7), very severe (2), or fatal (1), and the incubation period was 12 days in all of them. Among 10 cases classed as moderate (3), mild (4) or very mild (3), there were five in which the period was 15–17 days, in three it was 13 days, and in two it was 12 days. In one subclinical case it was 18 days.

Weil-Felix tests, carried out retrospectively on 25 other soldiers who had been exposed to similar risk, revealed that two of them had high titre reactions with *Proteus OXK* on the 28th or 29th day after exposure to risk : one of these soldiers gave a history of chilly feeling, headache and myalgia, lasting 12 days and starting 13 days after exposure ; his titre was 1–6,000 ; the other soldier had only headache and coryza, which lasted three days, after a presumed incubation period of 18 days ; his titre was 1–1,600.

It is stated that 55 cases of scrub typhus, contracted at the same time, were treated elsewhere, and that only one death occurred in the whole outbreak, in which at least 78 persons were attacked. *John W. D. Megaw.*

DAME, L. R. **Eye and Ear Sequelae of Scrub Typhus Fever.** *Bull. U.S. Army Med. Dept.* 1945, Nov., v. 4, No. 5, 554–7.

" Among 50 patients seen at a general hospital, convalescent (four to sixteen weeks, average six weeks) from scrub typhus fever, 50 per cent. of them had noticeable eye symptoms during the various stages of the disease, which proved to be transient and of minor importance. No permanent loss of visual acuity was found to be associated with this disease. In 98 per cent. of these eyes there were some abnormal subjective retinal findings, consisting of enlargement of the blind spots, contraction of the visual fields, and scotomata. The average size of all of the blind spots was 30 by 40 cm., and the largest 38 by 60 cm. There were 7 per cent. of field contractions, and 10 per cent. had scotomata, the largest being one-eighth of the visual field.

" Minor non-specific involvement of the cochlear system was found in only 11 per cent. of the ears at this stage of convalescence, although by history 78 per cent. of the ears had had hearing loss or tinnitus. All 50 patients had normal hearing with conversational tones. Involvement of the vestibular system was indicated in 59 per cent. of the ears with caloric stimulation. The mode of production and chronicity are not definitely known."

BRENNAN, J. M. **Field Investigations Pertinent to Bullis Fever. The Lone Star Tick, *Amblyomma americanum* (Linnaeus, 1758). Notes and Observations from Camp Bullis, Texas.** *Texas Reports on Biol. & Med.* 1945, v. 3, No. 2, 204–26, 3 figs. [17 refs.]

This abstract is supplementary to the one dealing with the author's preliminary note on the present investigations [see this *Bulletin*, 1945, v. 42, 799]. Full details are given of an exhaustive survey of *Amblyomma americanum* in the Camp Bullis area from June 8 to October 1, 1944. This tick has already been found infected with Rocky Mountain spotted fever, American Q fever and tularaemia in Texas. The chief object of the survey was to obtain large numbers of the tick for the further investigation of Bullis fever, with regard to which the author states that " it is quite likely that this disease is rickettsial " and that it is " a new rickettsial disease entity." [The latter statement will be considered by some workers as too dogmatic.]

More than 50,000 specimens of various stages of the tick were collected in the area, where it forms more than 95 per cent. of the total tick population, and where it is exceedingly abundant owing to the very large numbers of animals and birds which live in closely preserved conditions. In one case 294 of the

ticks, mostly adults, were found on a soldier; on the head of one deer 910 adults were found, and on the head of another there were 1,160 nymphs; larval forms were often too numerous to be counted. On occasions as many as one to three thousand larvae, but very few adults, were found on a fox, a jack rabbit, and a quail. Under a single small juniper tree four collectors picked up 4,086 adults from the thick litter of needle leaves on the ground, in the course of a single day.

The collection of unfed ticks by dragging the ground with a sheet of white flannel was found unsatisfactory; the plan adopted was to search for spots where the ticks were plentiful, a collector seated on the ground would often attract as many ticks as could be dealt with. Instead of using a cork for the collecting tube it was found better to tie a sheet of thin rubber, obtained from a discarded surgical glove, over the mouth of the tube and to cut a small slit in the rubber through which the ticks could be inserted by forceps. On completing the collection the rubber sheet was replaced by a plug of cotton wool.

The methods of collecting fed ticks from animals are described. Tables in the paper give full details of the infestation rates of the various hosts at different seasons. Every one of the 15 species of mammals examined was infested by ticks; the numbers on small rodents and on the armadillo were negligible. The dominant host of adult ticks was the deer, which also harboured large numbers of nymphs and larvae. The rabbit, fox, raccoon, skunk, and birds living on the ground or in thickets, were heavily infested by nymphs and larvae. Among the birds examined, 32 species were infested and 14 were non-infested.

The period of human infestation began in late February, the rate increased steadily till the end of May, declined slowly till the end of July, and then fell rapidly till the middle of August. From October to January, tick activity was negligible.

[Entomologists who have occasion to carry out tick surveys will find a great deal of useful information in the paper.] *John W. D. Megaw.*

Doerr, W. Morphologische Veränderungen bei Wolhynischem Fieber. [**The Morbid Anatomy of Trench Fever.**] *Münch med. Woch.* 1944, Sept. 22, v. 91, Nos. 35/38, 456–8. [10 refs.]

The changes described were found at the autopsy of a German soldier who killed himself by shooting on being discharged to duty from a hospital where he had been under treatment for two months for an illness diagnosed by competent physicians as trench fever. About seven months before this illness he had suffered from a moderately severe attack of typhus fever, and the changes observed after death could not be distinguished from those commonly resulting from typhus fever. The author himself admits that there is some doubt whether the lesions were due to typhus fever or trench fever, but he argues at some length in support of the view that trench fever was the cause.

*John W. D. Megaw.*

Stühmer, A. Das wolhynische "Periodische Fieber." [**Wolhynian "Periodic Fever" (Trench Fever).**] *Münch. med. Woch.* 1944, Aug. 11, v. 91, Nos. 31/32, 401–3, 1 chart. [11 refs.]

In 1916 the author published an article on "A New War Disease Resembling Relapsing Fever." In the present paper he describes an attack from which he suffered in 1916. The incubation period could be definitely fixed at 24–25 days. After three short spells of fever with a periodicity of about 7 days there was a long period in which only an occasional slight rise of temperature occurred. From the 12th to the 16th week fever of the undulant type occurred

with a periodicity of about 7 days. The illness lasted for three more weeks, during which there was hardly any fever, but there were three spells of pronounced tachycardia.

Recurring bouts of diarrhoea, great weakness, and severe shin-bone pains were the other chief features. *John W. D. Megaw.*

DAVIDS, B., Jr. Beobachtung einer Netzhautblutung bei Wolhynischem Fieber. [**Retinal Haemorrhage in Trench Fever.**] *Deut. med. Woch.* 1944, Aug. 4, v. 70, Nos. 31/32, 450–51, 2 charts.

A German soldier was admitted to hospital after having been in several other hospitals during the preceding month suffering from pain in the head, legs and especially the shins; a provisional diagnosis of Wolhynian fever [trench fever] had been made.

On admission he complained of poor vision, which he had first noticed while writing a letter about three weeks before. About a week before admission the sight of his left eye had become very bad.

On examination a large preretinal haemorrhage was seen, the rest of the retina and the bloodvessels being apparently normal. It gradually decreased in size during the following week and he was then transferred from the hospital.

He had no fever on admission nor afterwards, but during the previous month the temperature chart showed a curve resembling that of five-day fever [trench fever]. The differential diagnosis from typhus is discussed; the agglutination test with *Proteus OX19* was negative and there was no rash, while the appearance of the retina did not resemble the condition seen in typhus. As both his parents had died of apoplexy at about 70 years of age the author thinks that there may have been a constitutional tendency to vascular disease.

*J. F. Corson.*

RAETTIG, H. Die Pyriferbehandlung des Fünftagefiebers. [**The Treatment of Trench Fever by Pyrifer.**] *Med. Ztschr.* 1944, Dec., v. 1, No. 3, 101–2, 5 charts. [45 refs.]

The author states that his experience in the treatment of 50 patients with "pyrifer" [a proprietary colon bacillus vaccine for producing artificial pyrexia] confirms the favourable opinions expressed by RHEINDORF and other observers. He found that definite benefit resulted from a single injection in one-third of the cases, provided that the drug was administered during a febrile paroxysm. Repeated doses at intervals of two days gave no better results than a single injection.

The rationale of the treatment is believed by Rheindorf to be "an almost specific activation of the processes" [presumably of the immunizing mechanism].

No mention is made of the use of controls [see also this *Bulletin*, 1945, v. 42, 31]. *John W. D. Megaw.*

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## YELLOW FEVER.

EPIDEMIOLOGICAL INFORMATION BULL. (UNRRA Health Division.) Washington, D.C. 1945, Sept. 30, v. 1, No. 16, 687–92, 2 maps. **Third Report of the Expert Commission on Quarantine** [STOCK, P. G., Chairman].

The delineation of certain parts of Africa and the Western Hemisphere as endemic areas of yellow fever for quarantine purposes, recommended by the

Expert Commission on Quarantine of UNRRA, was adopted by the Standing Technical Committee on Health on 11th December 1944 ; since then the Commission has advised that certain additional areas should be included in the endemic zones.

In Africa the additional area is the Barotse Province of Northern Rhodesia ; in the Western Hemisphere the occurrence of cases of yellow fever in Venezuela and in the States of Minas Gerais and Goyaz in Brazil has led the Commission to recommend an alteration in the previous definition of the delineated areas.

The endemic areas are shown in the accompanying maps ; in South America the western boundary of the endemic area in Colombia and Peru passes along the eastern slopes of the Central Cordillera and the Andes Mountains at a height of 2,000 metres to the boundaries of Argentina and Bolivia.

African Yellow Fever Area delineated by Expert Commission on Quarantine.

[Reproduced from *Epidemiological Information Bulletin* (UNRRA Health Division.)]

South American Yellow Fever Area delineated by Expert Commission on Quarantine.

[Reproduced from *Epidemiological Information Bulletin* (UNRRA Health Division.)]

*J. F. Corson.*

DE PAULA SOUZA, G. H. **Yellow Fever Areas.** *Epidemiological Information Bull.* (UNRRA Health Division.) Washington, D.C. 1945, Sept. 30, v. 1, No. 16, 693–701. [10 refs.]

Under the International Sanitary Convention of Aerial Navigation, 1944, the nations concerned agreed to determine whether yellow fever existed in their territories, and the Expert Commission on Quarantine of UNRRA defined the endemic areas of the disease, *i.e.* where yellow fever " exists in a

form recognizable clinically, biologically or pathologically " ; these boundaries were specified for Africa and South America respectively [see above].

The mouse-protection test, viscerotomy, and the examination of animal and insect hosts for yellow fever virus were the methods used ; the last of these three methods caused the Ilheos and Itabuna districts in Brazil to be included.

The position is subject to revision from time to time and an area may cease to be considered endemic if satisfactory evidence regarding risk of infection and control of *Aëdes aegypti* is furnished.

The Pan-American Sanitary Bureau suggested to the Expert Commission that three classes of areas should be distinguished :—(1) Endemic areas where cases have occurred and where conditions favour its recurrence ; (2) areas where the risk of becoming infected exists ; (3) potentially infectible areas where an *Aëdes aegypti* index (*i.e.* the percentage of houses with breeding foci of *Aëdes aegypti*) of 0·4 or higher exists.

The National Department of Health of Brazil pointed out that the infected areas in Brazil varied in character, and suggested in detail certain modifications and exceptions.

More information about endemic areas is available for South America than for Africa ; in Brazil, in 1936, there were 1,559 viscerotomy posts and 32,031 liver samples were examined. In South America an *aegypti* index of 0·4 and less is attainable, while in Africa a goal of 1 per cent. is regarded as a good first step.

In the Western Hemisphere, the Central American countries west of the Canal Zone are no longer endemic areas, and the same applies to Mexico and the Caribbean islands ; in eastern Panama the endemic area approaches to within 50 miles of the Canal Zone.

No urban outbreak transmitted by *A. aegypti* has occurred in America since 1933 though *aegypti* transmitted yellow fever has often followed jungle yellow fever in Brazil, Bolivia and Colombia between 1934 and 1938, and once in 1942 in the Acre territory in Brazil. The risk of new outbreaks of *aegypti*-transmitted or urban-rural yellow fever in South America is now much reduced. A campaign against the mosquito is yielding good results ; in 1944 effective work was carried out in 44,859 localities with the result that 42,946 were completely freed ; *Aëdes aegypti* has been eradicated from eight States, and all dorts in Bolivia, Colombia, Ecuador, Paraguay and Brazil have an *aegypti* index of close to, or actually, zero.

Yellow fever still continues in endemic form or as wandering epidemics, shifting from one area to another, in vast jungle areas. No human case has been found around Villavicencio, Colombia, since 1938 and, from protection tests on local wild animals, it is thought that active virus no longer exists there. Similar shifting of areas occurred in Brazil. In 1945, an outbreak in the States of Goyaz and Minas Gerais, after quiescence for three years, caused 101 deaths in the first few months ; in July 1945, 18 deaths occurred in Venezuela and 14 in Colombia, while in May 1945, there were six deaths in Peru and two in Bolivia, east of the Andes in both countries.

In Africa knowledge is based chiefly on surveys ; in the western area which extends to the eastern border of Nigeria, *Aëdes aegypti* was the vector in urban outbreaks ; in the eastern area there is a zone of high incidence of human immunity situated between latitudes 3 and 8 N. and extending from the French Cameroons across French Equatorial Africa into the Anglo-Egyptian Sudan as far as Rumbeck. North and south of this zone there is a lower incidence of immunity. The Barotze Province of Northern Rhodesia is an inland endemic area.

For quarantine purposes endemic areas are extended to the Indian Ocean owing to the danger of eastward spread and the risk to India.

Extensive vaccination of persons exposed to jungle yellow fever, anti-mosquito measures, and prompt information of jungle infection, should make the defence against yellow fever complete. *J. F. Corson.*

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## DENGUE.

BOEHNHARDT, H. Ist das Bessarabienfieber eine neue Krankheit? [**Is Bessarabia Fever a New Disease?**] *Med. Ztschr.* 1945, Jan., v. 1, No. 4, 126–8. [15 refs.]

The author had described a short two-phase fever occurring in Bessarabia as a hitherto unknown disease [see this *Bulletin*, 1943, v. 40, 839]. He now replies at length to the adverse criticism of this view by MRUGOWSKY [see this *Bulletin*, 1944, v. 41, 968]. He makes out a strong case against the suggestion that the disease may have been trench fever or a fever of the typhoid group, but he admits that serious consideration must be given to the possibility of its being an aberrant form of sandfly fever.

[The controversy over this and other " new " short fevers in South-Eastern Europe is reminiscent of the many discussions relating to short fevers in tropical countries about 25 years ago. In both cases the diseases probably belong to the dengue-sandfly-fever group.] *John W. D. Megaw.*

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## PLAGUE.

MACKAY-DICK, J. **A Brief Report on Twenty-Six Cases of Bubonic Plague with the Results of Treatment.** *J. Roy. Army Med. Corps.* 1945, Sept., v. 85, No. 3, 105–8.

This report adds one more to the publications on the use of sulphonamide drugs in plague. Its purpose is to give the results of the treatment and to emphasize the desirability of early diagnosis and adequate treatment. Under these circumstances it is maintained that the mortality can be expected to be low. The 26 cases in this series are all set out in detailed tabular form, individually, with the precise treatment employed. This averaged 30 to 45 gm. of sulphapyridine per case, the sulphapyridine being combined with antiplague serum in 18 of the cases. The author insists that rest in bed should be strictly enforced, as in diphtheria, and the need for this appears to be exemplified by the occurrence of two sudden and unexpected deaths in patients who appeared to be out of danger. He is convinced of the value of sulphapyridine in plague, given either alone or in combination with antiplague serum. It is interesting to note that gland puncture " becomes negative after 24 hours of sulphapyridine therapy even when a positive result has previously been obtained."

*W. F. Harvey.*

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## CHOLERA.

STOWMAN, K. **International Quarantine Diseases. I. Cholera.** *Epidemiological Information Bull.* (UNRRA Health Division.) Washington, D.C. 1945, Aug. 15, v. 1, No. 13, 551–61.

An account of the distribution of cholera during the present century.

GRABAR, P. & GALLUT, J. Recherches immunochimiques sur le vibrion cholérique. IV. Essais de purification de la substance hypothermisante de la toxine cholérique. [**Hypothermy-producing Constituent of Cholera Toxin : its Purification.**] *Ann. Inst. Pasteur.* 1945, Sept.–Oct., v. 71, Nos. 9–10, 321–6.

The characters of the two constituents of cholera toxin were defined in a previous communication [this *Bulletin*, 1945, v. 42, 807]. Production of hypothermy and small molecular dimensions were the most notable of the properties found for the second constituent, purification of which is dealt with in this article under the headings : dimension of the molecule, antigenic power and chemical fractionation. A new technique is presented for its extraction, of which the detail is as follows :—Crude toxin of *p*H about 5·6 is precipitated with 1–5 ammonia, which occurs at about *p*H 8·6. This precipitate is washed several times with N/100 disodium carbonate until the supernatant fluid gives no precipitate with antiglucolipidic serum. It is then totally dissolved by N/10 hydrochloric acid at *p*H 3·5. In these attempts at purification the following characters have been established for the hypothermy fraction of the cholera toxin. It can pass cellophane membranes, has no antigenic power, is not precipitated by trichloracetic acid nor by sodium tungstate. Therefore it is probably not proteid (as the authors previously thought) ; it is probably a relatively small molecule, thermolabile, and liable to be carried down in the course of different precipitations. *W. F. Harvey.*

YACOB, M. & CHAUDHRI, J. R. **A Note on the Presence of 'O' Agglutinins in the Blood of Cholera Patients.** *Indian Med. Gaz.* 1945, June, v. 80, No. 6, 291–3.

Agglutinins may appear in cholera cases by the second day and are well marked by the sixth day. Their titre is not very high and the "O" agglutinins varied in the present series from 1 in 50 to 1 in 150. Little or no work seems to have been done previously on the persistence of these agglutinins, and that is the main object of the present enquiry. A knowledge of this point would be useful to the epidemiologist in case it were necessary "to conduct a late investigation of an outbreak of cholera in any locality." Thirty-seven cases were collected, with positive results in 13, and with the possibility of duration up to three and a half months, possibly more. *W. F. Harvey.*

INDIAN RESEARCH FUND ASSOCIATION. REP. SCIENT. ADVISORY BOARD FOR YEAR 1ST JAN. TO 31ST DEC., 1943, 1–7. **Cholera Treatment Enquiry under the Director, School of Tropical Medicine, Calcutta.**

The efficacy of sulphanilylguanidine in treatment and the preparation of pyrogen-free saline solution for injection are the two main subjects of enquiry. Every care seems to have been taken in appraising the value of the drug by the use of controls, although it is not stated definitely that they were strictly alternate. During the year sulphanilylguanidine was administered in 174 cases in the following doses : 5 gm. on admission, and 2·3 gm. every 4 hours after, to make a total of 20 gm. in 24 hours. A control series, also of 174 cases, is presented and this series by the criterion of proportion of patients with suppression of urine, was identical in number and character with the test series. Mortality was only 1·72 per cent. in the treated cases and 6·32 per cent. in the control series, a percentage which is markedly in favour of treatment by sulphanilylguanidine (sulphaguanidine).

Avoidance of accidental temperature and other reactions in the intravenous injection of saline solution is very important, and a careful series of clinical

trials and animal experiments with detailed record is presented, to furnish a satisfactory conclusion. As it was difficult to obtain freshly distilled water in quantity, measures were taken to make tap water pyrogen-free and suitable for injection. The method adopted was to acidulate 2,000 cc. of tap water with 0·4 cc. of 0·4 per cent. potassium permanganate and boil for 2 hours. If the permanganate tinge disappeared, more permanganate was added so as to maintain a trace of colour. At this stage the fluid can be stored, for no organism could grow in the acid water and produce pyrogen. At the time of use as saline solution this water was filtered through filter paper and 5–10 drops of hydrogen peroxide were added to it. Slight heating removed excess hydrogen peroxide and, when cool, the *p*H was adjusted to 7·1 with caustic soda solution. It may be concluded from the detailed experiments that " pyrogen free water can be prepared by treating water with acid potassium permanganate, as by the process of distillation." Other experiments were directed to the determination of optimum *p*H (7·1) and the effect of oxidizable matter on reaction following injection. The following conclusion is reached :—" The reactions following intravenous injections of saline solutions are due to pyrogen (a bacterial product), an oxidizable matter and higher or lower hydrogen ion concentration of the solution." *W. F. Harvey.*

Indian Research Fund Association. Rep. Scient. Advisory Board for Year 1st Jan. to 31st Dec., 1944, 1–4. **Cholera Treatment Enquiry under the Director, School of Tropical Medicine, Calcutta.**

Sulphaguanidine has already been tested and proved successful in the treatment of cholera, but as the trials were in patients seriously collapsed, transfusion of saline solution had to be used also and was a statistical complication. An opportunity has arisen in an epidemic of 97 cases to use sulphaguanidine early and to dispense with the saline solution. There were 53 cases thus treated, leaving 44 cases as controls. The results are recorded under the headings, recovered, died, unknown : for sulphaguanidine 79, 17 and 4 per cent. respectively, for the control series 25, 75 and 0 per cent. Vibriocidal and vibriostatic tests of sulphaguanidine with culture media showed that it had both properties, but that the bactericidal effect *in vitro* was poor.

Tests of another sulphonamide drug, sulphasuxidine [succinyl sulphathiazole] on serious cases requiring intravenous saline therapy with alternate case control were entirely disappointing. *W. F. Harvey.*

Gupta, S. K., Chatterjee, B. C., Paul, B. M. & Ghose, R. N. **Sulphanilylguanidine in Cholera.** *Indian Med. Gaz.* 1945, June, v. 80, No. 6, 288–90.

Preliminary trial had shown the harmlessness of sulphanilylguanidine (sulphaguanidine) and it was accordingly decided to try larger doses than previously. A large series of cases (525) of cholera was available, and 263 were treated with sulphaguanidine, the rest being alternate case controls. Saline transfusions were given in both groups as required. The dosage in these cases was : 5 gm. sulphaguanidine on admission and 2·5 gm. every 4 hours to reach a total of 20 gm. in 24 hours. Beneficial effect was quickly seen and, of 86 admitted with suppression of urine, 72 passed urine within 24 hours. This result is contrasted with that in the 72 patients of the control group, who also had suppression, of whom only 23 passed urine in 24 hours. Deaths among the 263 sulphaguanidine cases were only 3, whereas 13 out of the 262 controls died. A note is made of seven patients in the control group, not expected to recover and developing pre-uraemic symptoms, who did recover when given sulphaguanidine as a last resort. No case treated with sulphaguanidine

developed uraemia. Experiments were conducted also to show that sulphaguanidine had some vibriocidal and vibriostatic action *in vitro*.

*W. F. Harvey.*

Indian Research Fund Association. Rep. Scient. Advisory Board for Year 1st Jan. to 31st Dec., 1943, 9–21. **Enquiry on the Statistical Evaluation of Anti-Cholera Inoculation in the Madras Presidency under the Director, King Institute, Guindy, Madras, and the Director of Public Health, Madras.**

Up to the present day there have been very few sound statistical attempts to evaluate the effect of any prophylactic vaccine, nor does the present careful attempt for cholera conform to the requirement of the alternate case or the alternate village. It is, however, genuinely statistical and not impressionist. A very full account is given of the conditions under which the trial was made. According to Russell [this *Bulletin*, 1925, v. 22, 765 ; 1926, v. 23, 191 ; 1927, v. 24, 47] whose statistical study is one of the best, "the epidemiology of cholera in Madras Presidency is closely related to monsoons" and "there is a seven-yearly [six-yearly ?] periodicity when there is a marked exacerbation in the incidence of the disease." In Madras the last periodic wave, with 70,000 deaths, was in 1935–36 and it seems that the present wave began in the first quarter of 1942. Specially devised cards were printed for the present investigation, which applied to 2,300 villages of South Arcot. A total of 2,670 cards was obtained, relating to 1,283 villages in the district. The reality of immunization against cholera was the main fact studied. Certain special definitions are laid down to give precision to the results. The population of the 1,283 villages was 1,334,016, of whom 392,115 were protected by means of a single dose of Inaba-Ogawa vaccine. An incidence rate per mille of 1·5 for the protected and 17·1 for the unprotected was found which, for a 4-fold table, gives $\chi^2$ as 5478·7 and P less than 0·0016. The difference in incidence rates, as proof of immunity, is undoubtedly significant. Another important point which received attention was that of the time required to establish immunity by vaccination. For cholera a period of six days is prescribed in the International Quarantine Regulations. In the present epidemic it was found that "on each of the three days following the date of inoculation, the rate of incidence of cholera among the inoculated shows little variation ; this rate shows a progressive decline from the fourth day onwards and the minimum is reached on the 10th day after inoculation." The conclusion is arrived at that "uninoculated persons in a population at risk are susceptible to an extent of over 10 times in getting cholera as compared with the inoculated persons." When investigation is made of the benefit of vaccination to the inoculated person if he does contract cholera, it is found to be negligible. This field study is continuing.

*W. F. Harvey.*

Indian Research Fund Association. Rep. Scient. Advisory Board for Year 1st Jan. to 31st Dec., 1944, 4–21. **Enquiry on the Statistical Evaluation of Anti-Cholera Inoculation in the Madras Presidency under the Director, King Institute, Guindy, Madras, and the Director of Public Health, Madras.**

This enquiry follows very closely in method and in text that dealt with in the report of the previous year. It has, of course, larger figures to deal with, although the main findings are much the same. The protected persons are now 709,977 and the unprotected 2,119,568, with an incidence of cholera of 1·57 and 16·20 per 1,000 respectively. In this case the $\chi^2$ value is 9135·09

and P is less than 0·0016. In all, 2,350 villages were infected and 627 of these experienced more than one outbreak. The data obtained in the case of villages attacked more than once are used, for analysis of the effects of what are called "anticipatory inoculations," because the inoculation given in the first outbreak is considered, reasonably, capable of furnishing an answer to the question how far previous inoculation confers immunity. Again a significant difference is observed: "The incidence rate in the uninoculated persons was 14·2 times the rate in the anticipatory inoculations." A consideration of anticipatory inoculation leads on naturally to that of the duration of immunity conferred by anti-cholera inoculation. One method of arriving at a conclusion was to observe "the relative incidence of cholera in the uninoculated and the inoculated groups in a community in the course of an epidemic lasting for a sufficiently long time and noting the interval between the occurrence of cholera in the inoculated and the dates of inoculation." As it is difficult to find an epidemic lasting long enough to allow of this analysis, a better method is to study communities of inoculated and uninoculated persons where more than one outbreak has occurred in the community. A table gives the figures which, though small for statistical purposes, "point to the presence of immunity in the inoculated population definitely up to ten months and probably also up to twelve months after inoculation." *W. F. Harvey.*

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## BACILLARY DYSENTERY.

SCADDING, J. G. **Sulphonamides in Bacillary Dysentery. Further Observations on their Effects.** *Lancet.* 1945, Nov. 3, 549–53. [29 refs.]

Previously published observations [this *Bulletin*, 1944, v. 41, 755] suggested that patients suffering from bacillary dysentery showed no significant differences in the duration of their diarrhoea or their length of stay in hospital whether treated with sulphanilamide, sulphapyridine or sulphaguanidine. The present paper records further observations on the sulphonamide treatment of bacillary dysentery. Because sulphaguanidine is the standard drug for the treatment of this disease in the Middle East, first succinylsulphathiazole and then sulphadiazine were tested against sulphaguanidine; secondly, observations without controls were made on the effect of smaller doses of sulphadiazine; and, finally, a comparison was made of sulphaguanidine-treated and untreated control cases.

The disease was mild, and in cases where organisms were isolated, 75 per cent. were Flexner infections. The criteria of severity were the duration of diarrhoea before admission to hospital, the number of stools in the 24 hours before admission, and the incidence of fever. The results of treatment were judged by the duration of fever after admission, the duration of diarrhoea, and the total number of days spent in hospital. Treatment, besides sulphonamides, consisted of rest in bed, ample liquid intake, and a bland diet. No toxic complications of sulphonamide treatment developed throughout the investigation. Sulphaguanidine was given in a dosage of 7·0 gm. followed by 3·5 gm. four-hourly, reduced after 48 hours if the patient's condition had improved, the average total amount given being about 70 to 80 gm.

Succinyl-sulphathiazole, less well absorbed than sulphaguanidine, was given in a dosage of 2 gm. five times daily for 3 days, then four times daily for 4 days, the course being cut short if there was early improvement. With this course the durations of fever and diarrhoea were very similar to those of the patients treated with sulphaguanidine. The only differences were that the

sulphaguanidine-treated patients were in hospital, on the average, 1·3 days longer than those treated with succinyl-sulphathiazole, and showed a greater tendency to recurrence of diarrhoea during convalescence.

In the comparison of sulphadiazine with sulphaguanidine, the former drug, being readily absorbed, was used in dosage of 1·0 gm. five times daily, reduced after 48 hours if there was improvement, to thrice daily. The cases in the two groups were comparable in severity. Those treated with sulphadiazine had, on the average, slightly shorter fever and very slightly shorter duration of diarrhoea and of stay in hospital than those treated with sulphaguanidine. With reduced doses of sulphadiazine, down to 3 gm. daily, the results were little different, the duration of fever and of diarrhoea was very slightly longer, but the stay in hospital was rather shorter than in the series treated with larger doses.

In the series of control cases treated by rest and diet only, the mean duration of diarrhoea was 5·0 days, and of stay in hospital 12·3 days. The corresponding figures for alternate cases treated with sulphaguanidine were 4·4 and 10·8 days. The differences between treated and untreated groups were not statistically significant, but it is possible that in the figures for all cases a beneficial effect on a few severe infections was being masked by dilution with a large number of mild self-terminating ones, and in six Shiga cases there was suggestive evidence that sulphonamide treatment had proved beneficial.

The author gained the impression that sulphadiazine cut short long-continued bacillary-type dysentery on which the poorly absorbed sulphonamides had had no effect. He suggests that in these chronic cases the action of sulphonamides is to combat invasion of the bowel wall by secondary invaders, by virtue of their concentration in the blood, rather than on the dysentery bacilli by their concentration in the lumen of the bowel, where there are likely to be inhibitory substances. On this hypothesis action in acute cases is simply prophylactic against ulceration, either by the dysentery organisms or by the secondary invaders. This would explain the difficulty of detecting any differential effects in mild cases, the irregular response in severe cases, since the response will depend on what secondary invaders are prominent, and finally the fact that small doses of readily absorbable sulphonamides, which for other infections would be regarded as prophylactic rather than therapeutic, give as good results in acute bacillary dysentery as larger doses of the poorly absorbable compounds.

*F. Murgatroyd.*

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## AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

Druckmann, A. & Schorr, S. **The Roentgenological Manifestations of Amebiasis of the Large Intestine.** *Amer. J. Roentgenol. & Radium Therapy.* 1945, Aug., v. 54, No. 2, 145–8, 7 figs.

Where there is stenosis of the large bowel the radiologist should consider the differentiation of cancer and amoebiasis. Amoebiasis of the colon is either (1) diffuse or (2) localized. In the diffuse type the lesions scattered throughout the colon radiographically resemble those seen in idiopathic ulcerative colitis. In the localized type a more characteristic X-ray appearance is seen, in order of frequency, in the caecum, ascending colon, sigmoid and rectum. An opaque enema gives a more reliable picture than a barium meal.

The differentiation of a localized amoebic lesion of the large bowel from a cancer can be made on a number of grounds :—The amoebic lesion occupies an extensive segment of the gut ; the lesions in amoebiasis are frequently multiple, while the constriction of the bowel is relatively incomplete and is

expansile ; as a result, the passage of the barium through the constriction is not associated with pain—acute pain, due to the rigidity of the tumour, is a characteristic of malignancy ; the amoebic lesion shades into the normal gut gradually, the malignant abruptly ; haustration and mucosal relief are almost normal in the amoebic lesion ; and, finally, specific treatment largely or completely restores to normal the gut with a parasitic lesion.

Obstruction due to a neoplasm demands early operation, but in stenosis due to amoebiasis, surgery should not be resorted to. *A. R. D. Adams.*

HAWE, P. **The Surgical Aspect of Intestinal Amebiasis.** *Surgery, Gynecol. & Obstet.* 1945, Oct., v. 81, No. 4, 387–404. [43 refs.]

This paper reviews the types of intestinal amoebiasis likely to be met with in surgical practice in endemic areas, excluding distant complications, such as hepatic abscess. It is based on 450 cases of intestinal amoebiasis admitted to a British General Hospital in South India during 1942–44.

After a brief account of the pathology of the different types of amoebic lesion, the clinical aspect of each is described. Atypical forms of amoebiasis may simulate almost any gastro-intestinal disease and must always be considered as a possibility in patients who have lived in endemic areas. Diagnosis rests on finding the vegetative forms of *E. histolytica* in the stools or in scrapings obtained by sigmoidoscopy. The response to emetine is of considerable diagnostic significance, though occasionally in long-standing infections the condition may be resistant to the drug. If complete resolution is not obtained, the possibility of a coexisting lesion must be considered and exploration or biopsy is then required. Perforation of an amoebic ulcer is to be expected in less than 3 per cent. of cases, usually of a very severe type, but toxaemia may so mask the symptoms that the discovery of unsuspected perforations at the post-mortem examination is not uncommon. The bowel in acute cases is so friable that sutures will not hold, multiple perforations are common and the toxaemia is so overwhelming that the outlook, even with surgical interference, is grave. In subacute perforation an abscess may develop very insidiously.

The clinical features of acute caecal amoebiasis and acute appendicitis have much in common and a useful table of contrasting signs and symptoms is given. Important points are the previous history and the facts that in caecal amoebiasis the local signs appear earlier, are more diffuse and less constant in character and order of appearance than in acute appendicitis. On the other hand, an inflamed appendix in the high retrocaecal or the pelvic position may cause symptoms closely resembling those of amoebic dysentery. Every endeavour must be made to arrive at a correct diagnosis, as operation on cases of caecal amoebiasis carries special risks.

Chronic amoebiasis may occur in patients who give no history of dysentery and may give symptoms suggestive of appendicular disease. Suspicious signs are diffuse tender thickening of the caecum, tenderness over the sigmoid, or enlargement of the liver. In patients with a history of dysentery, it is important to remember that amoebic appendicitis is an extension of caecal amoebiasis and is a medical disease, unless complicated by abscess or perforation. Interval operation should be reserved for cases in which evidence of appendicitis persists after apparent cure of the caecal amoebiasis.

Localized chronic lesions with ulceration, thickening of the bowel and palpable mass may closely resemble carcinoma, tuberculosis, diverticulitis and other conditions. In the caecum they may cause a silent tumour, in the mid-colon obstructive symptoms, and in the lower part of the colon alternate diarrhoea and constipation. Radiological appearances give no pathognomonic picture, and diagnosis depends on the discovery of the amoeba and the diagnostic use of emetine.

In the rectum and anal canal, piles, fissure, fistula, ano-rectal abscess or perianal ulceration may coexist with or be caused by amoebiasis, whilst localized chronic ulcers in the rectum may closely resemble a neoplasm. Such cases are potential surgical catastrophes if their true nature is not detected. One example only of fibrous stricture was encountered.

The special risks of operations on the bowel in amoebic conditions are liability to an acute exacerbation of dysentery, supervention of local and distant septic complications, haemorrhage, delayed healing and failure of the intestinal suture line to hold. The author's conclusion is that operation is contraindicated in intestinal amoebiasis, except for perforation, abscess and obstruction, removal of an amoeboma which fails to respond to medical treatment, colostomy in rare cases of intractable ano-rectal fistula and possibly ileostomy in selected resistant cases.

[The addition of an analysis of the 450 cases which form the basis for this useful paper would have been of value.] *W. L. Harnett.*

Sodeman, W. A. & Lewis, B. O. **Amebic Hepatitis. Report of Thirty-Three Cases.** *J. Amer. Med. Ass.* 1945, Sept. 8, v. 129, No. 2, 99–104, 2 charts. [17 refs.]

The definition of amoebic hepatitis is one which embraces the earlier phases of amoebic hepatic disease before frank abscess can be diagnosed. All 33 patients in this series were adults, of whom 29 (88 per cent.) were men. Pain in the region of the liver was universal, varying from severe and sharp to dull and aching. Fever was present in all but one: in the more acute cases it reached 103° to 104°F., and was usually intermittent in type. What is termed "clinical jaundice" was present in 5 (15·1 per cent.). Other complaints, sometimes inconstant, were nausea, vomiting, weakness and loss of weight.

In 9 (27·3 per cent.), diarrhoea was present at the onset or during the course of the hepatic complication, or might antedate it for years.

The most important physical findings were hepatomegaly (in 88 per cent.), tenderness (in 100 per cent.) in the liver region. The total leucocyte count was elevated in 29 (88 per cent.) averaging 13,000. In 25 (75·8 per cent.), onset was distinct and sudden.

In three patients (9·1 per cent.) suspicion of pulmonary disease was based on the type of pain. In one this was referred to the right shoulder, and was accentuated by breathing; in the other two the pain, along the right costal margin near the mid-axillary line, was knife-like and suggested pleurisy. On the whole, however, in amoebic hepatitis the pulmonary picture does not attain the same importance that it does in certain cases of abscess.

In this group of patients with amoebic hepatitis a number of diagnoses were made, such as cirrhosis, cancer of the liver, acute and chronic cholecystitis, peptic ulcer, infective hepatitis, pyogenic liver abscess, carcinoma of the colon, pyelonephritis and pleuritis. In consideration of diagnoses the possibility of the occurrence of hepatic amoebiasis must always be kept in mind, even in those hospitals in which the conditions listed above are many times more common.

With amoebic hepatitis and jaundice, icterus indices as high as 70 were shown with positive urobilinogen tests; there were mild reductions in serum proteins in two, indirect van den Bergh tests in three, and impaired hippuric acid secretion and galactose tolerance tests in one patient each. The importance of radiographic examination, especially fluoroscopic study for impaired or paradoxical motion as well as elevation of the diaphragm, cannot be overemphasized, but pleurisy from any cause may impair diaphragmatic movement, and elevation of the diaphragm occurs in all forms of increased

intra-abdominal pressure as well as from infectious hepatitis and other forms of hepatomegaly. Some types of pulmonary disease, bronchostenosis for example, may give rise to paradoxical movement of the diaphragm. Also, in amoebic hepatitis the diaphragm may show no change if the upper portion of the liver is not remarkably involved. In the present group, abnormal radiological signs were present in only 15 (45·4 per cent.).

In only two was the complement fixation test of Craig carried out—one was positive, the other anticomplementary. There were difficulties in the way of carrying this test out as the material had to be sent away and a long time elapsed before results became available. *P. Manson-Bahr.*

Alecha, J. M., Carpanelli, J. B. & Ferreira, J. A. Absceso amebiano hepatico abierto en cavidad peritoneal. [**Amoebic Hepatic Abscess: Rupture into the Peritoneal Cavity.**] *Rev. Asoc. Med. Argentina.* 1945, Sept. 15, v. 59, No. 565, 1043–7, 1 fig. [44 refs.]

Marray, A. M. & Philipzs, G. C. L. **Report of a Case of Amoebic Abscess of Liver, Lung, and Brain.** *Glasgow Med. J.* 1945, Oct., v. 26, No. 4, 116–18.

Coutts, W. E. Uretritis por enteroparasitos. (Entameba histolítica y Lamblia intestinalis.) [*Entamoeba histolytica* **and** *Giardia intestinalis* **in Urethritis.**] *Rev. Chilena de Hig. y Med. Preventiva.* 1945, Mar., v. 7, No. 1, 3–5. English summary (9 lines).

The author relates that in an earlier publication he has called attention to the frequency with which trichomonas and spirochaetes can be detected in urethral discharges. In the present paper he describes two cases of urethritis, in the discharge of one of which *Giardia intestinalis* was discovered and in that of the other *Entamoeba histolytica*. In both cases a cure was obtained by injections of "pergonin". *C. M. Wenyon.*

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## RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Dewar, H. A. & Walmsley, R. **Relapsing Fever with Nephritis and Subarachnoid Haemorrhage.** *Lancet.* 1945, Nov. 17, 630–31.

The description of a fatal case of [presumably] tick-borne relapsing fever, in a soldier convalescent from amoebic dysentery. The patient had spent most of the previous four months in the western desert of Egypt.

The attack developed whilst he was still in hospital after his stools had become negative for *Entamoeba histolytica*, and treatment with carbarsone tablets (0·25 gm. twice daily by mouth) had begun. On the 5th day "*Spirochaeta recurrentis* was found in large numbers in a blood-film." On the 7th and 8th days the blood was negative, but the patient was severely ill and his blood urea rose to 390 mgm. per 100 cc. on the 10th day.

After only one bout of fever, nephritis and severe epistaxis supervened and the patient died on the 12th day as the result of a subarachnoid haemorrhage.

Autopsy was performed 2½ hours after death and attempts were made, without success, to detect the presence of spirochaetes in the bone-marrow, brain and spleen, both by examining smears and inoculation into mice. Microscopically, as well as *in vivo*, the most striking feature of the nephritis

was its intensely haemorrhagic character, which, together with the epistaxis and the perirenal and subarachnoidal haemorrhages, suggests a general haemorrhagic tendency in this case. *E. Hindle.*

[No information as to the species of tick responsible for transmission is given, and the evidence is presumptive only ; similarly, it is assumed that the organism was *S. recurrentis*, but no detailed investigation was possible.—*Ed.*]

LAHIRI, M. N. **Leptospirosis without Jaundice.** *Indian Med. Gaz.* 1945, July, v. 80, No. 7, 336–7.

The author describes the clinical symptoms of a patient, admitted to hospital for fever, headache and agonizing pains all over the body. He was seen on the eighth day of illness. The urine showed total absence of bile salts and pigments, but a trace of albumin was present. Cultures and animal inoculation of the patient's blood were negative, but the serum reacted to a titre of 1 : 1,280 with a local strain of leptospira.

A total of 225 samples of sera sent in to the Haffkine Institute, Bombay, for Widal tests were examined for leptospira by serological tests against three strains. One serum showed a titre of 1 : 640, and as it had been sent for Widal test jaundice was presumed to have been absent. *E. Hindle.*

MOHANTY, J. K. **The Occurrence of Leptospirosis in Orissa.** *Indian Med. Gaz.* 1945, July, v. 80, No. 7, 337–8. [11 refs.]

The record of a patient admitted to hospital for the treatment of haematemesis, melaena and jaundice. The agglutination reaction against a classical strain of *Leptospira icterohaemorrhagiae* was negative. Nevertheless the urine when centrifuged, showed the presence of spirochaetes closely resembling leptospirae. Animal inoculations were not possible. *E. Hindle.*

LAHIRI, M. N. **The Unsuitability of White Mice for Studies of Leptospirosis.** *Indian Med. Gaz.* 1945, July, v. 80, No. 7, 338–9.

Three-weeks-old Haffkine Institute inbred mice, and also Javanese mice, were inoculated with varying doses of two virulent cultures of *Leptospira icterohaemorrhagiae* in batches of three.

In the first series, out of 36 mice all survived except one, and in the second series of 30 Javanese mice there were only two deaths from the infection. In addition six " Swiss " mice were tested and all survived. The control guinea-pigs all succumbed between the fifth and seventh day after inoculation.

These experiments, therefore, do not support LARSON'S results (see *Bulletin of Hygiene*, 1942, v. 17, 144), at least so far as laboratory studies of leptospirosis in India are concerned. *E. Hindle.*

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## HELMINTHIASIS.

MAZZOTTI, L. Presencia de huevecillos de varios helmintos, diferentes del *E. vermicularis*, en la region perianal de individuos examinados en Mexico, para investigar oxiuriasis. [**The Presence of Ova of other Helminths in the Perianal Region of People in Mexico examined for Oxyuriasis.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, June, v. 6, No. 2, 131–5. English summary (4 lines).

The examinations were made in four seaside localities with a tropical climate and in Mexico City which has a temperate climate ; 1,260 schoolchildren were

examined in the former places and 1,229 children and 500 adults in Mexico City. GRAHAM'S method with Scotch cellulose tape [this *Bulletin*, 1942, v. 39, 780; 1943, v. 40, 617] was used.

The results are given in detail in a table. Among the 2,989 persons examined, helminth ova other than those of *Enterobius vermicularis* were found in 198 (6·6 per cent.); they included ova of *Ascaris lumbricoides* (96), *Trichuris trichiura* (100), hookworm (6), *Taenia* (26), and *Hymenolepis nana* (3).

The children in the tropical localities had a greater incidence (up to 20 per cent.) than the persons in Mexico City (2·8 per cent.). The author discusses the point whether the proglottides of *Taenia solium* migrate through the anus.

*J. F. Corson.*

McMULLEN, D. B. & BEAVER, P. C. **Studies on Schistosome Dermatitis. IX. The Life Cycles of Three Dermatitis-producing Schistosomes from Birds and a Discussion of the Subfamily Bilharziellinae (Trematoda: Schistosomatidae).** *Amer. J. Hyg.* 1945, Sept., v. 42, No. 2, 128–54, 1 fig. & 3 pls. [35 refs.]

"1. Techniques used in detecting schistosome infections in birds are described.

"2. In experiments with three dermatitis-producing schistosome cercariae, *C. physellae* Talbot, *C. elvae* Miller, and *C. stagnicolae* Talbot, adult schistosomes have been recovered from birds. After examining these trematodes and the literature on members of the subfamily Bilharziellinae Price, 1929, the adults of *C. physellae* Talbot were determined as *Trichobilharzia physellae* (Talbot) (syn. *Pseudobilharziella querquedulae* McLeod) n. comb.; the adults of *C. elvae* Miller as *Trichobilharzia ocellata* (La Valette) (syn. *T. kossarewi* Skrjabin and Zakharow); and the adults of *C. stagnicolae* Talbot as *T. stagnicolae* (Talbot) n. comb.

"3. A revision of the generic diagnosis of *Trichobilharzia* is proposed. This reduces the genus *Pseudobilharziella* Ejsmont to synonymy with Trichobilharzia. Since it is difficult to differentiate species in this genus on the basis of adult morphology it is concluded that the eggs may be one of the most reliable characters for this purpose.

"4. While no attempt has yet been made to find these three common species in resident or migratory birds in the vicinity of infested beaches, it is evident from earlier studies that the most common natural hosts are migratory birds, and the present study has shown that *Trichobilharzia ocellata* and *T. physellae* develop in ducks and other birds while *T. stagnicolae* was found to reach maturity in canaries only.

"5. In all three species eggs are produced in about 2 weeks after infection and there is some evidence that the infection does not last longer than 1 or 2 months.

"6. Protecting beaches from flocks of migrating birds, especially in the fall, may be of value in preventing schistosome dermatitis on bathing beaches."

HARRIS, J. R. & HICKEY, M. D. **Occurrence of the Diphyllobothriidae in Ireland.** [Correspondence.] *Nature.* 1945, Oct. 13, 447–8.

This paper further discusses the occurrence of plerocercoids of Diphyllobothriidae found by the authors [this *Bulletin*, 1944, v. 41, 858] in trout in Poulaphouca reservoir, near Dublin; by DUGUID and SHEPPARD [*ibid.* p. 857] in trout in a South Wales reservoir; and by GIBSON [*ibid.* 1945, v. 42, 396; see also UNSWORTH, *ibid.* p. 397]. BAYLIS [*ibid.* p. 906] has examined adult Diphyllobothriids reared experimentally in dogs from the Dublin and South Wales

plerocercoids and considers that all these plerocercoids and also the adults obtained from gulls and cormorants by the authors mentioned above probably belong to the Diphyllobothriid species, *D. dendriticum* (Nitzsch) which is normally parasitic in gulls, although those found in the cormorants may be *D. ditremum*. The possible confusion of the plerocercoids of these bird species with those of *D. latum* of man required further investigation, because it is very difficult to distinguish from one another the plerocercoids of different species of Diphyllobothriidae. The difficulty is increased in Eire, because *D. latum* does occur there. Harris and Hickey here record references to its occurrence, the first record being that of Bellingham—and O'Bryan—(*Ann. Mag. Nat. Hist.*, 1844, v. 14, 251). To these records Harris and Hickey add another recent one. They received from Dr. T. V. McLoughlin a specimen of *D. latum* recovered from a boy aged 14, who had eaten perch from Gardice Lake, Co. Leitrim. Harris and Hickey searched 79 perch from this lake for plerocercoids and found from 1 to 8 plerocercoids per fish in 35 of the 79 perch examined. Similar plerocercoids were found in two perch from Lough Allen, Co. Leitrim. Plerocercoids from the Gardice Lake perch were given by mouth to two adult dogs and from both of these dogs, which were given 2 and 8 plerocercoids respectively, adult Diphyllobothriids were recovered. The two adults obtained from the dog given 2 plerocercoids were specimens of *D. latum*.

Harris and Hickey compare the plerocercoids obtained from trout of Poulaphouca reservoir, Dublin (namely those of *D. dendriticum* of gulls or *D. ditremum* of cormorants) with those from the perch from Gardice Lake, from which they experimentally reared *D. latum*. They note the following differences :—

The plerocercoids of *D. latum* were opaque and dull white and were only sluggishly motile ; they seldom relaxed sufficiently to lose their typical irregular, deeply-wrinkled appearance. When they were killed in tap water, the scolices usually remained invaginated and showed deep wrinkles. Of the 81 plerocercoids found in the perch of Gardice Lake, 71 were found in the skeletal muscles and only 10 in the peritoneal cavity or abdominal viscera. There was no inflammatory reaction around them.

The plerocercoids of the trout from Poulaphouca reservoir (of the bird species) were translucent, glistening white and actively motile. They showed no wrinkling, except when they were strongly contracted. When they were killed in tap water, they invariably relaxed and evaginated and wrinkles were never present, although some showed segmentation. Out of the 198 infested trout examined, only one had plerocercoids in the skeletal muscles (two were found in it) ; in all the others the plerocercoids were in the viscera or subserous tissues of the abdominal cavity. Around them there was often an inflammatory mass of blood-stained granulation tissue.

The authors examined fish from other Irish waters, namely, reservoirs in Wicklow and Dublin Counties, Lough Mask, Co. Mayo, four Lakes in Connemara, Co. Galway and Lough Esk, Co. Donegal. Plerocercoids superficially resembling those found in trout from Poulaphouca reservoir (*i.e.* presumably plerocercoids of Diphyllobothriidae parasitic in birds and not in man) were found in trout (*Salmo trutta*), salmon (*S. salar*) and char (*Salvelinus colii*). *G. Lapage.*

Graña, A. Alergia y diagnóstico biológico de la hidatidosis. [**Allergy and the Biological Diagnosis of Hydatid Disease.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1945, June, v. 26, No. 6, 538–59. [75 refs.] English summary.

It is not possible to abstract in detail this review of an extensive bibliography of this subject. The author considers much South American work which is not readily accessible and also incorporates his own experience. Many

of the papers considered are also reviewed by TALIAFERRO (*The Immunology of Parasitic Infections*, 1929, Century Co., London and New York).

In the course of his discussion of the technique and significance of the immediate and delayed (Casoni) intradermal reaction, Graña reminds us that tuberculosis is among the conditions other than hydatid disease which may give rise to falsely positive intradermal reactions to the injection of hydatid fluid. He quotes the work of DABOWSKY (cited by MOLLOW, see this *Bulletin*, 1931, v. 28, 205), who obtained a high percentage of positive intradermal reactions with hydatid fluid in tuberculous children [*cf.* DAVIS, HARRELL and KING, *Bulletin of Hygiene*, 1946, v. 20, 673]. Graña states that statistics show that positive Casoni reactions are most numerous in subjects with hydatid cysts of the liver and next most numerous in those with cysts of the lung. In his experience strongly positive Casoni reactions may occur even when hydatids of the liver and lung are suppurating or are calcified; but they are often negative in subjects with cysts in the bones or brain.

The technique and significance of the Prausnitz-Küstner test applied to hydatid disease is discussed. Graña obtained a positive Prausnitz-Küstner reaction in only one of many subjects who gave a strongly positive Casoni intradermal reaction; but he considers, nevertheless, that the passive transference of hypersensitivity is possible.

Human hydatid fluid has, he considers, a very low antigenic power. The sterile cysts of the liver and lung of sheep give the best hydatid fluid for use as antigen. Fernandez ITHURRAT and CALCAGNO [see this *Bulletin*, 1924, v. 21, 208] obtained, however, just as good results with human hydatid fluid as with fluid obtained from oxen and sheep; they maintain that the antigenic power of the fluid should be tested both on healthy subjects and on subjects with hydatid cysts before it is used. Discussing the nature of the substance which provokes the intradermal reaction, Graña recommends for use either 0·1 cc. of hydatid fluid previously tested, or the protein fraction obtained by DENNIS (*J. Parasitology*, 1937, v. 23, 60), who isolated a protein by precipitation with 5 per cent. trichloracetic acid and obtained with it intensely positive reactions with erythema prolonged for 48 hours, and oedema lasting 4 to 5 days. [See also the polysaccharide and protein obtained and tested by PIROSKY *et al.* (this *Bulletin*, 1943, v. 40, 474).]

The author next discusses the blood eosinophilia and the local eosinophilia which may both result from the injection of small amounts of hydatid fluid into subjects with hydatid cysts. In hydatid disease the blood eosinophilia is not significant unless it exceeds 5 per cent.; but values higher than 5 per cent. may occur when infestations of the muscles and blood with other parasites are present and also when there are skin affections, allergic conditions, etc. [*cf.* DIXON and HARGREAVES (this *Bulletin*, 1945, v. 42, 907) who discuss the results of their study of 284 cases of cysticercosis due to *Taenia solium* and quote the opinion of GOTOR (this *Bulletin*, 1943, v. 40, 65) that Continental workers have attached too much importance to blood eosinophilia, which Dixon and Hargreaves found in only 10 per cent. of their cases; they agree with MACARTHUR, (this *Bulletin*, 1934, v. 31, 384) that such deviations from the normal eosinophilia of the cerebrospinal fluid as may occur have no diagnostic significance, and that the cerebrospinal fluid generally remains unaffected even when there is gross cerebral cysticercosis. Graña, on the other hand, refers in the paper here reviewed, to the view of PARVU and LAUBRY (*C.R. Soc. Biol.*, 1909, v. 66, 467) that "the eosinophilia of the cerebrospinal fluid which is so characteristic of cerebral cysticercosis" (see GRAÑA & SCHENONE, this *Bulletin*, 1942, v. 39, 705, and SELMAN, *ibid.*, 1945, v. 42, 816) is not present in hydatid disease. Graña insists that both the relative and the absolute eosinophilia of the blood must be considered. He found that the subcutaneous or

intradermal injection of even as much as 10 cc. of hydatid fluid did not cause, in healthy subjects, a significant increase of eosinophils in the blood, but, in subjects with hydatid disease, repeated injections of hydatid fluid caused eosinophilia in proportion to their sensitivity as indicated by the degree of the Casoni reaction. One subject tested by Graña showed a local eosinophilia so intense that the fluid in the local blister contained 29 per cent. of eosinophils. Although MOLLOW (*loc. cit.*) does not attribute diagnostic value to this induced eosinophilia, Graña considers that it has real diagnostic value if it is considered in relation to the other blood changes provoked.

The author next reviews some of the literature on the complement fixation (Ghedini-Weinberg) reaction. Like the Casoni reaction it may give false positives in subjects suffering from haemangioma or primary cancer of the liver (see MOLLOW, *loc. cit.*). PARVU and LAUBRY (*loc. cit.*) record that, in subjects with cerebral hydatids, the complement fixation reaction done with cerebrospinal fluid is positive, although it is negative when it is done with blood.

Discussing heterophil antibodies, Graña refers to the work of CALCAGNO (*Boletines y Trabajos de la Acad. Argent. de Cirurg.*, 1939) who studied the effects of the injection of hydatid fluid into subjects harbouring hydatid cysts and called this procedure the " biological therapy " of hydatid disease [*cf.* RIVAS, GÓBICH and MANTILLA, this *Bulletin*, 1945, v. 42, 910]. Graña (*Dia Méd.*, Buenos Aires, 1943, v. 14, 1092) [see also this *Bulletin*, 1944, v. 41, 764] has observed in the serum of subjects thus treated a notable increase of haemolysins and agglutinins for the erythrocytes of sheep, and has obtained agglutination in dilutions of serum as high as 1 : 2,048, and haemolysis in dilutions of 1 : 4,096, using the technique of PAUL and BUNNELL (*Amer. J. Med. Sci.*, 1932, v. 183, 90) for the diagnosis of infectious mononucleosis. Graña noted great variability in the titres of heterophil antibodies shown by different individuals harbouring hydatid cysts in relation to the same antigen. He has found [this *Bulletin*, 1944, v. 41, 764] that in rabbits and in subjects without cysts injection of hydatid fluid does not cause an increase of agglutinins and haemolysins to erythrocytes of sheep, while in subjects with cysts the rise in these heterophil antibodies is strictly parallel to the degree of hydatid allergy shown by the Casoni intradermal reaction done upon them. Graña (*Arch. de Med. Cirug. y Especialidades*, 1944, v. 24, 471, and *Clinica e Immunologia*, Edit. Espasa Calpe, 1944) found that the formation of these heterophil antibodies is rapid and intense and that this serological reaction has a certain diagnostic value (see also Graña, *Medicina*, Buenos Aires, 1945, *in the press*). Graña has also seen a notable increase of agglutinins and haemolysins to sheep erythrocytes in the sera of sensitive subjects into whom extracts of *Ascaris lumbricoides* of the pig have been injected (*Rev. Brasileira Biol.*, 1945, v. 5, 81). The author then describes what he calls the triple response to the introduction of antigen. If the eosinophilia exceeds 5 per cent. and the intradermal and complement fixation reactions are positive, one can be sure that the subject has a hydatid cyst. If all or some of these reactions, including titration of the serum against the erythrocytes of sheep, are negative, and if we wish to increase the efficacy of the reactions, the triple response can be tried. Hydatid fluid (2 cc.) is injected intradermally into separate sites in the skin each day for five days ; if after 96 hours, or, with more certainty, after 48 hours, from the beginning of the reaction, a negative complement fixation reaction has become positive and the eosinophils have exceeded 5 per cent., it is necessary to suspect hydatid disease, because subjects without cysts do not react in this way in so short a time (see Graña, *Arch. de Med., Cirug. y Especialidades*, 1944, v. 24, 471, and *Medicina*, Buenos Aires, 1944, v. 4, 290). Five to ten days after the last injection the late response shown by increase of agglutination

of sheep erythrocytes is studied, and if the titre of this is above 1 : 32 by the technique of Paul and Bunnell there is further reason for the diagnosis of hydatid disease.

The author next discusses histaminaemia in hydatid allergy. Graña *et. al.* (*Medicina*, Buenos Aires, 1943, v. 3, 98) found that histaminaemia in subjects with hydatid disease is very variable. High values were found in subjects with hepatic hydatid, three of whom had calcified cysts. One subject with a small calcified hydatid had marked digestive troubles and his histaminaemia rose to the titre of 48 gammas per cent. Such high values suggest a relation to the increased number of eosinophils in the blood, for Code (*J. Physiology*, 1937, v. 89, 257) suggested that the eosinophils carry the histamine. Randolph and Rackemann (*J. Allergy*, 1941, v. 12, 450) could not, however, accept this view, and Graña and his collaborators found no relation between the absolute or relative number of eosinophils and the degree of histaminaemia, nor did he find histamine in the vesicle produced by injection of hydatid fluid, although in this there were 29 per cent. of eosinophils.

Clinically, subjects with hydatid disease can show various signs of classical allergy, such as asthma, urticaria, angioneurotic oedema and other symptoms which rapidly yield to desensitization with hydatid fluid. The author refers to instances of asthma which were clearly of hydatid origin and to the provocation of a severe asthmatic state by the injection into a subject with a hydatid cyst of the lung of excessive quantities of hydatid fluid. Jaureguy and Soto (*Alergia hidatica pulmonar*. Monografia. Imprenta Rosgal, Montevideo, 1941) interpret radiological shadows in the lung near a hydatid as of hydatid origin. There are many instances of chronic and stubborn urticaria which have vanished when the hydatid cyst has been removed. In one subject cited by Graña it disappeared after the first desensitizing injection of hydatid fluid. Various other symptoms may also disappear after similar injections. Among the most notable results of this biological therapy (see Calcagno above) is the rapid disappearance of dyspeptic pains and symptoms of a hepatic of biliary type in subjects with calcified liver hydatids and without any lesion of the gall bladder (*cf.* Graña, *Bol. de la Soc. de Cirurg. de Montevideo*, 1943, May; and *Dia Méd.* Buenos Aires, 1943, v. 14, 1092, and *Prensa Med. Argentina*, 1944, v. 31, No. 16).

Discussing anaphylactic shock due to the rupture, accidental or during surgical operations, of hydatid cysts and the consequent rapid and massive absorption of antigen by subjects previously sensitized, the author quotes the view of Chauffard *et al.* (*C.R. Soc. Biol.*, 1909, v. 67, 499) that this sensitization is slow and chronic, being produced by the passage of hydatid fluid through the wall of the intact cyst or through small fissures in the cyst. Death may result from this shock. D v [illegible] (*Rev. de Chir.*, 1911, v. 1, 153) describes post-operative hydatid "intoxication", which corresponds to anaphylaxis due to reabsorption of hydatid fluid; this kind of phenomenon does not occur during operation, because the general anaesthesia inhibits the signs of shock, which may be benign or severe. Graña suggests that the study of experimental shock shows that hydatid fluid is a primary toxin to cells, and it is possible that what is interpreted, in man, as pure anaphylaxis may be a combined result of anaphylactic phenomena and primary toxicity of hydatid fluid.

The author then discusses experimental hydatid anaphylaxis and reviews literature on this question which shows, he thinks, that there has been difficulty in producing experimental anaphylaxis. Lemaire thinks that this difficulty may be due to the fact that hydatid fluid is poor in proteins. Dessy and Marotta (*Rev. de la Soc. Med.*, 1912, v. 20, p. 373) produced shock in dogs by the intravenous injection of 20 cc. of hydatid fluid, and Giusti and Hug (*II° Congreso de Medicina*, Buenos Aires, 1922, v. 1, 691) confirmed this and also

produced shock by injection of hydatid fluid which had been either boiled or ultrafiltered. They found that the histamine titres were so small that the effect of this substance could be ignored. Graña has confirmed the results of Giusti and Hug. Graña and his colleagues (*Rev. de la Soc. Argent. de Biol.*, 1943, v. 19, 444, and *Amer. J. Physiol.*, 1945, v. 143, 306) showed that in some dogs the histamine increased in the blood during the shock, while in others the histaminaemia increased, so that histamine could not have been the cause of the shock. A substance can, however, be extracted from hydatid cysts which is responsible for the shock ; this is not a protein ; it is resistant to heat and is precipitated by acetone. A dose of 60 mgm. produces in dogs a profound shock which is followed by desensitization. *G. Lapage.*

Davis, O. T., Harrell, G. T. & King, E. S. **The Effect of Simultaneous Tuberculous Infection on Experimental Trichinella Infestations in Guinea Pigs.** *Amer. J. Med. Sci.* 1945, June, v. 209, No. 6, 758–64, 3 figs.

This paper is reviewed in *Bulletin of Hygiene*, 1945, v. 20, 673.

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## DEFICIENCY DISEASES.

Trowell, H. C. & Muwazi, E. M. K. **Severe and Prolonged Underfeeding in African Children. (The Kwashiorkor Syndrome of Malignant Malnutrition.)** *Arch. Dis. in Childhood.* 1945, Sept., v. 20, No. 103, 110–16, 5 figs. [30 refs.]

The name " kwashiorkor " is a tribal word from the region of Accra in the Gold Coast, and is not understood outside this area, but the syndrome for which it stands is found in many parts of Africa and possibly elsewhere. This syndrome includes a pale red skin with brownish hair, a " crazy pavement " dermatosis, wasting, oedema, anaemia, lowered plasma albumin and raised globulin, a gastro-intestinal defect seen radiographically as gross segmentation of the small gut, and marked fatty degeneration of the liver. In its advanced stages the syndrome is notably refractory to treatment. The syndrome has frequently been taken to be a manifestation of pellagra, but this view is no longer tenable. The anaemia, at least in Uganda, is macrocytic and hypochromic ; megaloblasts are seldom, if ever, seen in films of peripheral blood or bone marrow.

Adding to the previous descriptions of the senior author, Trowell and Muwazi during 1945 examined 180 children, 126 of them out-patients and 54 in-patients, at Kampala, Uganda. After the sixth month about three-quarters of all cases attending the clinic showed signs of the syndrome. Plasma proteins were determined in 20 patients ; in most cases the plasma albumin was low and the plasma globulin was high, so that the albumin/globulin ratio was low : in every case this ratio was below the mean albumin/globulin ratio for normal children ; in many cases it was less than 1.

Malaria parasites were found in 119 of the 180 children. Among these same children were 17 probable cases of congenital syphilis. Of the 54 cases in the wards of the hospital, 12 had pneumonia, 4 bacillary dysentery, 1 amoebic dysentery, 14 ankylostomiasis, 4 ascaridiasis, and 6 giardiasis. Thus in the tropics " kwashiorkor " is seldom seen uncomplicated by infection, of which the most important is malaria. The syndrome has, however, been observed in South Africa almost uncomplicated by tropical disease.

The authors think that the syndrome may be the same as severe marasmus in European children, with a few variations due to the peculiarities of the

African diet. They also point out that it is almost impossible to distinguish the syndrome from coeliac disease, although in " kwashiorkor " oedema is far more common and many more cases proceed rapidly to inanition and death.

A trial of desiccated hog's stomach in six cases gave encouraging results : one case is described in some detail. This child, who had severe oedema, showed no improvement during a fortnight on a high-calorie, high-protein diet plus thiamin and nicotinic acid, nor during a further 4 days with daily injections of liver extract. Desiccated hog stomach given by mouth was followed by a remarkable and rapid improvement. [See also GILLMAN *et al.* this *Bulletin*, 1944, v. 41, 1057 ; 1945, v. 42, 748 ; 1946, v. 43, 59.]

The authors suggest that the syndrome should be called " malignant malnutrition."

*H. E. Harding.*

QUITTER, F. Beiträge zum Pellagraproblem. [**Contributions to the Problem of Pellagra.**] *Deut. Tropenmed. Ztschr.* 1944, Jan. 1, v. 48, Nos. 1/2, 18–25. [11 refs.]

The author is convinced that pellagra in Rumania presents several differences from the disease elsewhere ; so much so that he regards the so-called pellagra in some of the Balkan districts as pseudo-pellagra and not true pellagra at all. In Rumania the disease was present where maize was much used, and when other grains took its place pellagra diminished. On the other hand cases are seen in Rumania in which maize plays no part, and the disease is seen in the better nourished and well-to-do families. In Rumania the disease is typically seasonal ; cases begin to appear at the end of February and the beginning of March, and increase until the summer, when they begin to fall in numbers ; by late autumn and the start of winter they disappear altogether. The symptoms typically are tiredness, apathy, and later—often much later—glossitis, burning sensations in the throat, digestive disturbances, erythema of hands, feet, face and neck. There may be no relapse the following year, even though the patient remains at home and in no way changes his mode of living. Mental disturbances appear late.

The author does not regard pellagra as purely an avitaminosis, because it is rare to see more than one case in a family (of 79 patients in 1941 only two were members of one family) and cure takes place without increase of vitamin intake. There may be a " constitutional endocrine factor " and some cases clear up quickly when sexual hormones are given. In others there is evidence in favour of some sensitizing factor, as photosensitivity ; the gastritis may be of a " constitutional " nature, when relapse is likely to occur, or it may be accidental and fortuitous and, if so, once cured it is not likely to return. Allergic diseases are commoner in females, says the author, and 91 per cent. of his patients were women, and treatment with specific anti-allergics, as Reticulin or Torantil [both are prepared from animal tissues], yielded good response. The allergy might be endogenous (auto-intoxication) or exogenous, perhaps due to some toxin in spoiled maize.

The author quotes several cases which improved on Reticulin. One, a severe case, may be cited. A man, aged 20 years, ill each spring for the past two years, worse this year ; is apathetic and will not answer questions ; has erythema of the face, lips swollen and painful, tongue has many painful fissures, burning sensation in throat and stomach, such that he can take scarcely any food. He was given Reticulin, 2 cc. every other day, and improvement started after the fifth injection ; the throat and stomach symptoms were eased, the general state was better and three weeks after completion of the course the hands and feet showed only slight pigmentation ; he was much more alert and his only complaint was of feeling fatigued sooner than he used to at his work.

The author regards nicotinic acid as having the properties of a vitamin; daily administration of 200–300 mgm. led to definite improvement in 12–14 days. It is not an anti-pellagra vitamin but acts as a constituent of cozymase.

Other patients were treated with Decholin, 10 cc. injections of 20 per cent. strength, on alternate days. Here again an example may be quoted: a man of 53 years, with lassitude, erythema, glossitis, gastritis, severe diarrhoea, burning pain in the throat. Six injections were given. At the end of the first week his subjective symptoms were vastly improved and by the end of the course he was "in general cured"; some redness of the skin remained, but that was all.

Neither those treated with Reticulin nor those with Decholin changed in any way their mode of living, so that the results may definitely be ascribed to the treatment adopted. *H. Harold Scott.*

NICHOLLS, Lucius. **Tropical Nutrition and Dietetics.**

This book is reviewed on p. 165.

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## HAEMATOLOGY.

DENHOFF, E. **Hematologic Values of American Soldiers Stationed in the Tropics.** *J. Lab. & Clin. Med.* 1945, Oct., v. 30, No. 10, 874–82.

American medical officers stationed in the South-west Pacific had more than once remarked in general terms that "each month the red blood cell count seems to be lower and the incidence of eosinophilia increases." The author resolved to put this supposition to the test and examined the blood of 655 American soldiers admitted to hospital and of a small number (33) of healthy soldiers. The former included 142 who had been stationed in the tropics for 6 months, the main causes for admission to hospital being bacillary dysentery and acute infective hepatitis; 211 who had been out for 12 months, the causes of admission being respiratory diseases, bacillary dysentery and malaria; and 302 who had been out for 18 months; filariasis and malaria were the main diseases in these. In these three groups respectively the average red cell counts and haemoglobin estimations (by the Tallqvist scale) were 4,710,000 per cmm. and 88 per cent.; 4,560,000 and 86 per cent.; and 4,390,000 and 84 per cent. As regards the controls, the average of 14 recent arrivals was 4,970,000 and 95 per cent. haemoglobin, and of these together with 19 others after a year's stay 4,770,000 and 91 per cent.; at the end of two years the average was 4,400,000 and 84 per cent.

Among those in Group I, there was only one (0·7 per cent.) noted as a case of "borderline normocytic anaemia"; in Group II there were 13 (6·7 per cent.) and in Group III 29 (9·6 per cent.). Eosinophilia of 9 per cent. or over was present in 1, 7 and 26 (or 0·7, 3·3 and 10·1 per cent.) respectively in the three groups, accounted for by helminthic infestations or dermatoses; for 9 others no explanation was found.

Of 100 patients garrisoning filaria-free islands, 8 had this degree of eosinophilia, while of 156 on an island where filariasis was endemic 18 (11·5 per cent.) had eosinophilia. Of 140 healthy soldiers on filaria-free islands 5 (3·5 per cent.) had eosinophilia compared with 40 (28·1 per cent.) of 142 exposed to filariasis.

It will be seen, therefore, that the erythrocyte count and the haemogobin values fell with length of service, and it was thought that lack of thiamin, riboflavin and ascorbic acid were contributory factors. Monotony and lack

of palatability of the food were also part causes, the food itself being adequate. The incidence of true anaemia was slight. It is noteworthy that a high incidence of eosinophilia was present in healthy soldiers who had been stationed in a filaria-endemic island, although they presented no clinical evidence of infestation. [See also this *Bulletin*, 1945, v. 42, 1020.] *H. Harold Scott.*

HOLMES, E. G. **Observations on Oedema occurring during the Course of Macrocytic Anaemia.** *Brit. Med. J.* 1945, Oct. 27, 561–4.

Oedema and ascites in tropical macrocytic anaemia have usually been attributed to cardiac insufficiency, but in the present series of 38 cases of macrocytic anaemia in East African troops in the S.E. Asia Command, oedema and ascites, which occurred in 12, did not appear, except in one, until, as a result of treatment, the blood count had risen considerably, and at a time when other signs which could be attributed to cardiac decompensation were entirely absent. As the manufacture of haemoglobin involves the synthesis of protein as well as the production of the iron-containing haem molecule, observations were undertaken to ascertain whether any diminution in plasma protein occurred which might explain the oedema and ascites in such cases. Oedema is said to occur if the total protein falls below 5·5 per cent., or the albumin below 2·5 per cent. The osmotic pressure of the serum depends upon the sum of the osmotic pressures of its albumin and globulin components. The albumin is the smaller molecule, and is said to exert about four times as much osmotic pressure as the globulin. The albumin/globulin ratio taken alone has no particular significance; it may be low because of increased globulin, and a serum in which the albumin is decreased and the globulin normal or raised may therefore exert a lower osmotic pressure than a serum of equal or less total protein content but containing a higher proportion of albumin. From the Tables given in the paper it would seem that oedema in tropical macrocytic anaemia is not explicable solely on a basis of low serum protein.

Although the response to treatment was slow, the average duration being 105 days, the majority of patients were ultimately returned to duty in Category A. Treatment consisted of a daily diet, of about 4,000 calories, containing 165 gm. protein, of which 38 gm. was derived from meat (muscle), 22 gm. from liver, 31 gm. from milk, and 12 gm. from eggs. In addition, each patient received 2 to 4 oz. of a marmite substitute, vitamin tablets, iron, and sometimes 2 oz. of yeast. Some also received liver extract orally or by injection; in only two so treated was a reticulocyte response observed. Two patients showed a reticulocyte response to the marmite substitute. Eight patients had one or more blood transfusions because of their precarious condition, while five of the oedematous patients received intravenous infusions of reconstituted serum. This latter treatment was followed by diuresis, and in three cases the oedema and ascites began to clear up a few days later; in the other two it seemed to have little effect. In cases with effusions not causing serious mechanical embarrassment, paracentesis was considered undesirable because it involves loss of protein to the body.

The method used for serum protein determination was based on that of WALTHER (*Lancet*, 1941, Sept. 20, 337) but in the absence of a colorimeter, a Lovibond tintometer with a blood urea disk was used. The serum non-protein nitrogen estimations were not entirely satisfactory, the colour comparison often being hindered by cloudiness, but fortunately the protein equivalent of the N.P.N. is small and the inaccuracy involved not material; when the N.P.N. is high the difficulty disappears since greater dilutions can be used. Fractionation of the albumin and globulin was carried out on the usual principles with sodium sulphate; in the absence of suitable filter paper the clear supernatant solution was pipetted off after standing. *F. Murgatroyd.*

ROSENBAUM, S. **Chronic Leucopenia in Childhood.** *Harefuah.* Jerusalem. 1945, Oct. 15, v. 29, No. 8. [In Hebrew 188–91. English summary 191.]

" Chronic leucopenia (5,500 and fewer leucocytes per cmm.) was found in 13 per cent. of 880 children. Chronic ' decided leucopenia ' (50% and less of the normal leucocyte values for the corresponding age) was found in 3%, chronic lymphocytopenia (50% and less of the normal lymphocyte counts for the corresponding age) in 1·7%.

" 62·5% of these children were underweight.

" Chronic leucopenia may be either congenital or acquired. Familial cases were observed.

" The condition may continue for years.

" In one-third of the cases there was an eosinopenia. But considerable eosinophilia may be observed. The eosinophilic system reacts by itself, independent of the granulocytic or lymphocytic system.

" The percentage of eosinophiles, not the total eosinophile count is characteristic of an allergic reaction.

" Chronic leucopenia is in the vast majority of the cases a sign accompanying a transient or permanent inferiority of one or more functional systems. These children suffer from catarrhal diathesis, muscular weakness, neuropathic and psychopathic conditions, and allergic affections are also relatively frequent. Nutritional disturbances due to digestive insufficiency and lambliosis may produce chronic leucopenia. In two cases premature birth may have been the cause.

" Chronic ' decided leucopenia ' and chronic lymphocytopenia correspond in their pathognostic significance entirely to chronic leucopenia. In febrile infections there is an increase in the white blood cells. But this increase is relatively moderate. The children react within the limits of their diminished leucocytic reactive power. In purulent conditions, the granulocytes are chiefly increased, in catarrhal infections, chiefly the lymphocytes.

" The sulfonamide drugs and salicylic acid do not seem to be a special danger in the sense of agranulocytosis. Nor have spontaneous agranulocytoses been noted."

WEINGARTEN, R. J. **Influence of Temperature on Sedimentation-Rate : its Clinical Significance.** *Lancet.* 1945, Oct. 27, 526–9, 3 figs.

The influence of temperature on erythrocyte sedimentation rate was investigated because experience suggested that the common belief, that high external temperatures accelerate and low temperatures retard the rate, was false. In the investigation, the Westergren method was used with all technical precautions. Readings were taken every ten minutes, blood was withdrawn with as little venous stasis as possible, the patients having been kept fasting. Comparative determinations were made at 99°F. and at 44°F. ; preliminary experiments showed that previous chilling or warming of the specimens did not materially influence the rate in the actual determinations.

Of 483 miscellaneous cases examined, 279 (57·7 per cent.) showed a higher sedimentation rate at 99°F., 109 (22·7 per cent.) showed a higher rate at 44°F. and 95 (19·7 per cent.) showed less than 10 per cent. difference between the rates at the two temperatures at any stage during an hour. Thus the general statement that erythrocyte sedimentation rates are raised at higher temperatures is not correct.

In patients with hepatic disorders an increase in sedimentation rate at low temperatures was most pronounced, readings in the first 10 minutes often being more than five times as high in the cold as in the warm environment. In the

cold, the fall of the corpuscles was very rapid during the first 30 minutes, slowing down only as packing prevailed. In all these cases the clumping of the erythrocytes into large visible aggregates was remarkable, occurring usually a few minutes after the tubes had been placed in the cold. This phenomenon was very pronounced in a case of blackwater fever, sedimentation being complete in under two minutes. *F. Murgatroyd.*

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## VENOMS AND ANTIVENENES.

Boquet, P. Sur les propriétés antivenimeuses du sérum de *Vipera aspis.* [**The Antivenene Properties of the Serum of** *Vipera aspis.*] *Ann. Inst. Pasteur.* 1945, Sept.–Oct., v. 71, Nos. 9–10, 340–43.

The blood of the common viper of France is toxic, but the symptoms it produces are not the same as those set up by the venom. The venom is a blood-coagulant and contains a phosphatidase enzyme capable of transforming lecithin into haemolytic lysocithin. The serum is haemolytic owing to its direct action on the red corpuscles and is not a coagulant, and the toxicity of the serum is not affected by antivenene. Again, the serum when heated to 58°C. loses its toxicity but neutralizes the venom as strongly as the best antivenenes prepared by a long course of immunization of horses. It also neutralizes, at least to some degree, the venoms of other Viperidae : *Bitis arietans, Cerastes cornutus, V. russellii* and *Bothrops atrox.*

Venom and antivenene combine to form an insoluble product, but the admixture of serum and antivenene does not result in any precipitation. Nevertheless, the neutralizing property of the viper serum is derived from the venom ; it is thought that a small part of the venom, in the course of its elaboration in the parotid, gains entrance to the blood like an internal secretion. This is at variance with the idea that a substance can be antigenic only if it is foreign to the organism. *H. Harold Scott.*

Del Pozo, E. C., González Q., J. & Méndez, T. H. Acciones del veneno de alacran sobre el aparato respiratorio. [**The Action of Scorpion Venom on the Respiratory Apparatus.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1945, June, v. 6, No. 2, 77–84, 4 pls. English summary.

Sergent, Et. Sérothérapie antiscorpionique (Huitième note). Observations médicales reçues pendant l'année 1944. [**Anti-Scorpionic Serotherapy. Eighth Note : 1944.**] *Arch. Inst. Pasteur d'Algérie.* 1945, June, v. 23, No. 2, 111–14.

Since 1936, of 1,739 cases of scorpion sting reported, 470 were regarded as dangerous to life and were treated with serum. The percentage of recovery was 89·3 (420 subjects). [See this *Bulletin*, 1945, v. 42, 404.]

Kirby-Smith, H. T. **Specific Treatment of Black Widow Spider Bite.** *Southern Med. J.* 1945, Oct., v. 38, No. 10, 696–8.

" It is the conclusion of the writer that the treatment of black widow spider bite with black widow spider antivenin administered a comparatively short time after the bite is successful in relieving pain and preventing its recurrence."

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## DERMATOLOGY AND FUNGUS DISEASES.

BAGBY, J. W. **A Tropical Lichen Planus-like Disease.** *Arch. Dermat. & Syph.* 1945, July, v. 52, No. 1, 1–5, 6 figs.

The author states that, since the beginning of the war, numerous cases of a disease which in its clinical appearance is suggestive of lichen planus have been noted on some tropical islands of the Pacific. In some instances the disease begins as true lichen planus; in others, as a generalized, erythematous, exfoliating eruption, the efflorescence of the primary lesions being followed by the appearance of localized lichenoid papules. A third group is described in which the primary lesions are bullae, which are replaced by papules or nodules simulating hypertrophic lichen planus. Usually the distribution is generalized, but in several cases the mid-portion of the trunk has been free from lesions. The face, scalp, palms and soles may be involved, also the tongue and buccal mucosae. As the eruption retrogresses, pigmentation of the affected areas is noted; in some instances the residual lesions are atrophic, depressed, deeply pigmented scars.

The clinical histories of five cases are recorded, and details and illustrations of the results of histological examinations are given. All the patients were white men; all except one—who was 27 years old—were aged from 42 to 47. Their period of tropical service had varied from 2 to 19 months. All except one had taken 0·1 gm. of quinacrine hydrochloride [mepacrine] daily; the exception had received this drug and quinine [doses not stated] for an attack of malignant tertian malaria which had subsided seven days before the eruption appeared. Most of the men had lost weight before the lichen developed. The author notes that the eruption tends to improve when the patient is *en route* to the United States; he has not seen the malady in negroes. He adds the following comments:

1. Several men with lichen planus were seen in the eastern part of the Solomon Islands in 1943, but none with this atypical form was observed. Many more cases of this eruption have appeared in 1944 than in 1943, though the administration of quinacrine hydrochloride and the dietary allotments were the same for both years.

2. Various forms of lichen planus had been observed long before quinacrine hydrochloride came into use.

3. I have administered quinacrine hydrochloride to five men nearly well of the disease, giving each three tablets daily for four days (admittedly a short trial), without causing a flareup of their lesions.

4. The eruption has none of the features usually associated with dietary deficiencies or with drug eruptions.

5. The disease has appeared in men who had been in the tropics for only two or three months, in which period it is not likely that severe avitaminosis would occur.

[This paper is important, as it is believed to be the first which has been published concerning a malady that has attracted the attention of military dermatologists and malariologists serving in sub-tropical and tropical areas. Medical Officers serving with the British Forces have only recently been permitted to submit their observations on this disease for publication. It will be noted that whilst the author indicated that quinacrine hydrochloride is a common factor in all cases, he does not attribute the eruption solely to this cause. Those interested in the matter may care to trace the following references: *Arch. Dermat. & Syph.*, 1944, v. 49, 224, and 1945, v. 51, 353; also *Lancet*, 1945, Dec. 1, 711.] *R. M. B. MacKenna.*

Berger, L. Beadry, M. & Gaumond, E. **Chromoblastomycosis due to a New Species of Fungus (First Canadian Case).** *Canadian Med. Ass. J.* 1945, Aug., v. 53, No. 2, 138–42, 6 figs. [10 refs.]

The authors give a careful survey of the history of chromomycosis and describe a new case ; the first example of the disease recorded in Canada.

The lesion of chromomycosis generally affects only one region ; in 90 per cent. of cases it is on the lower extremity, because of its greater exposure to trauma. In the Canadian case, however, the lesions were multiple and widely distributed. The granuloma appeared first on the web between the 4th and 5th fingers of the left hand and, on reaching the size of a hazel-nut, it was excised after an erroneous diagnosis of prickle-cell carcinoma. A month later it reappeared and spread all over the dorsum of the left hand, while secondary granulomata appeared on the left forearm, the right hand, the left foot, the buttocks, the right cheek and the right ear. The lesions consisted of thick, warty, cauliflower-like masses of pink, brown or violet colour, with a more or less moist surface from the continual oozing of a foul-smelling exudate. Histologically the granuloma did not differ essentially from that seen in typical chromomycosis, but the yeast-like form of the parasite in the tissues was relatively small, usually thin-walled and showed budding forms and chains of cells, whereas the common fungi of chromomycosis (*Phialophora verrucosa* and *Hormodendrum pedrosoi*) appear in the lesion as thick-walled cells, often septate but never budding. In culture, the fungus from the Canadian case grew freely on the common media used in mycology, as brown or black yeast-like colonies of creamy consistency. The microscopic morphology of the fungus in culture presented the characters of the genus *Candida*, but, because of its black colour, Emmons and Carrion considered it to be related to *Pullularia pullulans* (syn. *Dematium pullulans*). The authors are, however, contented for the present to consider the strain as " a black Candida-like, but still unnamed new species."

Treatment consisting of intensive iodine and X-ray therapy, autovaccination with the fungus, and local injections of arsenic and methylene blue was without avail. After two years of fruitless chemotherapy the lesions were removed by amputation, electrocoagulation and scraping. The subsequent history of the case is not yet available. *J. T. Duncan.*

Levy, B. M. **Chemotherapy of Experimental Histoplasmosis in White Mice.** *Amer. J. Trop. Med.* 1945, May, v. 25, No. 3, 241–51, 8 figs. [47 refs.]

Up to the present time no drug treatment has been found effective in histoplasmosis ; the following have been used without success—Fuadin, Neostam, sodium iodide, neoarsphenamine, bismuth, pentnucleotide and liver extract, sulphanilamide, sulphathiazole, sulphapyridine, atabrine [mepacrine], Prontylin, potassium arsenite, quinine, emetine, Sulpharsenal, vitamins and other remedies.

As, apparently, no chemotherapeutic experiments had been made on artificially infected animals, the author undertook this work and, using a freshly isolated strain of *Histoplasma capsulatum*, he inoculated, intravenously, 145 young white mice with the living culture. The inoculum was prepared by grinding up and suspending in sterile isotonic saline, a seven-days-old culture on blood-agar at 37°C., consisting of the mixed mycelial and yeast forms of the fungus. The density of the suspension was adjusted to equal that of " No. 4, McFarland barium sulphate standard," and the infecting dose used for intravenous injection was 0·2 cc. Within 24 hours of inoculation, treatment was started by injecting, by the peritoneal route, appropriate doses of the following drugs in sterile solution : sodium iodide, Neostam, Fuadin,

sulphanilamide, proflavin, thymol, B-9 (an organic iodide) and sodium propionate. All the animals in the eight groups developed histoplasmosis and in no case had the drug any observed effect on the course of the disease.

*J. T. Duncan.*

✓ da Silva-Lacaz, C. Contribución brasileña para el estudio de la " blastomicosis sud-americanas " (Granulomatosis paracoccidioidica). [**Brazilian Contribution to the Study of Paracoccidioidal Granuloma.**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1945, Aug., v. 27, No. 2, 167–81. English summary.

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## HEAT STROKE AND ALLIED CONDITIONS.

Borden, D. L., Waddill, J. F. & Grier, G. S., III. **Statistical Study of 265 Cases of Heat Disease.** *J. Amer. Med. Ass.* 1945, Aug. 25, v. 128, No. 17, 1200–205, 8 figs. [13 refs.]

This is an incomplete study of heat casualties occurring among troops undergoing training in a southern coastal area of the United States. In the summer of 1942, there were four fatal cases of heat stroke ; in May to September 1943, 265 cases of effects of heat (" heat disease ") were admitted to hospital [the total population at risk is not stated] ; there were three fatalities. For statistical purposes, the cases seen in 1943 were divided into two main groups " mild " and " severe," but the proportion of the one to the other is not reported. An analysis of cases according to age, amount of training and home State, southern or northern, is given, but the corresponding distribution of the total population is not stated. For treatment, the division was into group 1—cases without circulatory failure and with cramps, and group 2—cases with circulatory failure. The former group is labelled by the authors " Heat Prostration," and apparently about 14 per cent. of all the cases came under this category. The second and larger group were all regarded as exhibiting different degrees of the same pathological process. The milder cases showed mainly circulatory collapse and were called " heat exhaustion." The more severe cases showed hyperthermia and were called " heat stroke " [it is not obvious that any real " flash " hyperpyrexias or heat strokes were seen, though the history of one of the fatal cases is suggestive]. Nearly all cases showed some pyrexia.

The treatment of the group 1 patients was by rest and sedatives, cooling by water spray and by fan, water and salt orally in all cases and intravenous saline in severe cases ; 0·9 per cent. saline intravenously was found to be specific for the relief of cramps. In the group 2 patients who showed evidence of shock, plasma transfusions were given rather than saline, to avoid the danger of pulmonary oedema ; pure oxygen was given in all severe cases. Patients with definite hyperthermia were cooled by spraying and ice bags. All cases of effects of heat were considered to be emergencies and the patients were taken to a special treatment room immediately on admission, and later transferred to an air-conditioned recovery ward. [The Americans here are following the practice adopted by the British Army in Iraq in 1941, of having special heat stroke centres in all hospitals equipped with air conditioning, and of having air-conditioned wards available for heat and other cases.] Pathological findings are not reported in detail here but are promised later. Post-mortem findings on three fatal cases in 1943 showed widespread petechial haemorrhages in brain, intestine, lungs and blood vessel endothelium, and passive congestion in liver and lungs [similar findings have often been reported before].

The authors consider that all " heat disease " is due to heat accumulation resulting from inadequate evaporation when heat losses from convection, radiation and conduction are minimal owing to a high dry bulb temperature. They, therefore, believe that the wet bulb temperature is a good indicator of the probable incidence of heat disease, particularly at low wind velocities ; they show charts correlating wet- and dry-bulb temperature and heat cases over the three hottest months of the year, in support of this view. Accordingly, in 1943 the physical activities of the troops in this area were limited on hot humid days and close order drill and severe training were stopped when the dry bulb temperature was 88°F. or over, and the wet bulb 77°F. when the wind velocity was above 10 miles per hour, or—if the wind velocity was below 10 miles per hour—when the wet bulb thermometer was 75°F. or over. It is not stated whether this measure gave a reduced instance of heat casualties as compared with that in 1942. The troops were advised to drink 500 cc. of 0·1 per cent. saline each hour while at exercise in the heat, and patients with heat exhaustion who gave a history of not taking the prescribed amount of salt were subjected to appropriate disciplinary action.

[This is a useful study, but unfortunately it does not go into sufficient detail. The statistical information is inadequate, and the account of the symptomatology is very compressed, *e.g.* there is no indication of the degree of pyrexia in the various cases other than that their temperatures were above 99·6°F. The association of symptoms is not considered at all. The promised pathological report should, however, be interesting.] *W. S. S. Ladell.*

BLUM, H. F. **The Physiological Effects of Sunlight on Man.** *Physiol. Rev.* 1945, July, v. 25, No. 3, 483–530, 4 figs. [261 refs.]

The author's thesis is that all the evidence points to the physiological effects of sunlight on man being detrimental rather than beneficial. With the exception of the effect on avitaminosis D, sunlight, and even ultra-violet light, is probably nothing more than a good *placebo*.

The spectral distribution of sunlight is from wavelengths less than 0·3$\mu$ to beyond 2·1$\mu$. The distribution is affected by passage through the atmosphere ; the ultra-violet in particular is absorbed by ozone and small dust particles, hence there is most ultra-violet all the year round in the tropics, where the ozone is least, and little ultra-violet in the winter in temperate regions because the air mass is then greater and there is most ozone. The visible spectrum is not much affected by these factors, hence it may seem to the eye to be as bright at 5 p.m. as earlier in the day, but sunburning, which is due to the ultra-violet, will not occur owing to the greater air mass through which the radiation passes. Similarly, a fine dust haze will screen off the ultra-violet without any visible diminution in intensity ; on the other hand, diffusion by dust and water droplets gives rise to sky radiation which is rich in ultra-violet light, so sunburning will occur on an apparently overcast day.

On reaching the skin up to 45 per cent. of the total sunlight is reflected if the skin is white, but only 16 per cent. if it is black ; the major portion of the rest is absorbed before it has penetrated more than a few millimetres. The maximum penetration is with wavelengths between 0·7 and 1·5$\mu$ ; HARDY found only 6 per cent. transmission of infra-red radiation through two millimetres of human skin. With wavelengths below 0·32$\mu$ transmission is also very low ; the radiation is scattered by dead cells in the corneum and absorbed by the protein of the cells, so none is transmitted and not much reflected. Radiation of wavelengths of 0·5$\mu$ is not absorbed in the corneum ; some is reflected and some gets through to the blood vessels beneath, where it is absorbed by the haemoglobin. Wavelengths of 0·6$\mu$ are not absorbed by

haemoglobin and get through to subcutaneous tissues. Longer wavelengths than are found in the sun's radiation are all absorbed superficially. In the eye, maximum transmission is of radiation at wavelengths $0{\cdot}8\mu$; in general, penetration is deeper and there is no scatter. The ultra-violet is absorbed by the protein in the coats and media; and in the infra-red there is zero transmission with wavelengths $1{\cdot}4\mu$, owing to absorption by the water of the aqueous and vitreous; but enough infra-red can get through to the retina to cause burns—" eclipse blindness "; it is dangerous to look at the sun through glasses which filter off visible radiation only. The retinal pigment absorbs all radiation that reaches it.

Most of the radiation is absorbed non-specifically and heats the skin. Sunlight gives rise only to thermal sensations; the greatest intensity of sunlight (0·03 gm. cal. cm.$^2$ sec.) is not sufficient to give rise to pain. The stimulus for thermal sensation is an alteration in the temperature gradient in the skin, hence the infra-red which is absorbed superficially, gives the best effect; so radiation from a hot stove is a more effective stimulus than sunlight. Negroes, whose skins are better absorbers of sunlight, have a lower sensory threshold to it than have whites. The radiant energy absorbed on the skin may raise the surface skin temperature above the body temperature, especially if the circulation to the skin is diminished or stopped so that distribution of the heat to the rest of the body by the blood-stream cannot occur. The solar heat load on a naked body may be large and equal to the metabolic heat load of walking at 3 miles per hour; it is more for negroes whose skin does not reflect so much of the sun's radiation, but in all cases it can be reduced by clothes. It does not vary much with latitude as there is only 20 per cent. difference in intensity of the total radiant energy from the sun between the sun at zenith and the sun at 60° from zenith.

The chief photo-chemical effect of sunlight is sunburn. After about half an hour's exposure to sunlight (the exact threshold for intensity and for time varies greatly between individuals and at different times) there is a latent period, after which erythema and a slight swelling develop. With longer exposures there is marked oedema followed by desquamation and blistering. Later, the erythema gives place to tanning and finally the sun-tan itself darkens with further exposure. The erythema is produced solely by rays of shorter wavelength than $0{\cdot}32\mu$, *i.e.* by ultra-violet light; the time the erythema takes to develop varies with different wavelengths. No histological changes are found before the erythema appears. Blum considers that the first action of the ultra-violet is on the cells of the Malpighian layer. Comparison between the action spectrum and the respective absorption spectra indicates either cell protein or nucleic acid as the light absorber; Blum favours the protein. There are some discrepancies between the action and the absorption spectra but these can be satisfactorily explained. The ultra-violet light produces in the cells a dilator substance which differs somewhat from the H substance; Menkin (*J. Exper. Med.*, 1936, v. 64, 485) has called this " leucotaxin." This substance diffuses down to the papillary vessels, hence the latent period between exposure and erythema. Leucotaxin increases capillary permeability, causing oedema, and exerts a chemotactic effect stimulating the migration of leucocytes out of the vessels. This hypothesis is supported by the finding of an increased concentration of dilator substance in the skin and blood of animals after ultra-violet radiation. The cells of the epidermis degenerate either owing to a direct affect of the ultra-violet or, according to Menkin (*Arch. Pathology*, 1943, v. 36, 269) as the result of the production of another substance, " necrosin ". The longer wavelengths of the erythema spectrum may also penetrate far enough to have a direct effect on the papillary vessels. There is not yet any explanation of the continuation of the erythema for a long period without further exposures.

The erythema is replaced by sun-tan. The sun-tan spectrum is the same as the erythema spectrum. First there is a migration of melanin granules from the basal cells to more superficial layers, and then there is formation of fresh melanin in the melanoblasts. Though melanin can be formed *in vitro* by the action of ultraviolet light, in the presence of ferrous salts, on tyrosine, this process requires more ultra-violet than can reach the basal cells in sunlight and cannot take place without free oxygen, whilst sun-tanning can occur in skin deprived of oxygen. Bloch (*Ztschr. Physiol. Chem.*, 1916, v. 98, 226; *Amer. J. Med. Sci.*, 1929, v. 177, 609) however, finds dopa-oxidase in cells injured by ultra violet light and suggests that melanin is formed in them from L-dopa (laevorotatory β 3–4 dioxyphenylalanine) brought to them by the blood stream.

After the sun-tan has developed, radiations of wavelength up to 0·42$\mu$ cause a further darkening of the tan without formation of more melanin. This darkening occurs more rapidly than the initial tanning and may be due to oxidation of a reduced leuco-melanin as it will not occur in the absence of oxygen. This longer wavelength radiation is not stopped by glass and is also present in winter sunlight, hence the retention of sun-tan by some individuals throughout the winter. A similar darkening of pre-formed melanin can be brought about by the administration of sex hormones.

A sun-tanned skin gives some protection against sunburn; this is due primarily to a hyperplasia of the cells of the corneum after ultra-violet irradiation, and the thick layer of cells that results shields the sensitive basal layer from further irradiation. When the corneum regains its original thickness, most of the immunity passes off, though the sun-tan remains. There is, however, some protection from absorption of the ultra-violet light by the melanin which has migrated superficially; this is the cause of the relative immunity of negroes to sunburn. In addition, there is some cellular immunity to the action of ultra-violet light, which develops 12 hours after exposure. Sweat and sebum have no effect on the erythema threshold, but artificial protection against sunburn will be given by any substance that absorbs the wavelengths concerned, *i.e.* from 0·29 to 0·32 $\mu$.

The belief that exposure to sunlight can cause tumours comes from the observed greater incidence of cutaneous cancer among outdoor workers and on areas of exposed skin; this belief is supported by the observation that malignant tumours develop in rats and mice after ultra-violet irradiation. The carcinogenic rays are of the same wavelengths as the erythema rays. The action of the ultra-violet light is either direct injury of the cells or the induction of somatic mutations by its action on nucleic acid. There is a discrepancy in that, in mice, the tumours are sarcomata, whereas in man they are carcinomata; this is explained by the thickness of human skin, which is so great that the radiation cannot penetrate to the connective tissue beneath. Cutaneous cancer is certainly more common, according to Dorn (*Pub. Health Rep.*, Wash., 1944, v. 59, pp. 33, 65 and 97) in latitudes where there is more ultra-violet; thus, at 41°N. the incidence in the United States of America is 23·1 per 100,000, but 9° further south it is 116·4.

The action of the ultra-violet radiation on certain steroid compounds to provide vitamin D in the skin takes place in the corneum, and considerable amounts of the vitamin may be lost in desquamating cells after irradiation. The release of leucotaxin or of some vasodilator substance is probably the cause of a fall in systemic blood pressure observed after sunburn and after irradiation from a carbon arc, which has a similar spectrum to sunlight. No direct effect of sunlight on metabolism and growth has been found. The sexual cycle of certain animals is affected by light probably because, with longer illumination, waking hours are longer and there is greater activity. Cook (*New*

*York J. Gynec. & Obstet.*, 1894, v. 4, 282) described suppression of menstruation in Esquimaux women during the dark Arctic winter, but this has not been confirmed.

Excessive sunlight on the eyes causes photo-ophthalmia ; this is simply sunburn of the eyes. Very long wavelength radiation will produce cataract (glass blowers' cataract) and also intense ultra-violet irradiation of the lens might injure it and give rise to opacities, but the high incidence of senile cataract in countries near the equator is probably not due to insolation.

Certain dyes and naturally occurring pigments have a photo-dynamic action; when introduced into living systems they render the cells photo-sensitive so that oxidative processes, usually injurious, take place on exposure to light. Porphyrin pigments are photo-dynamic and as they may be derived from plants, grazing animals are sometimes affected, and this may be of great economic importance in some regions ; but man is rarely directly affected in this way.

Though sunlight is a major factor in man's environment it is not so by direct physiological action. It is easy to escape from a solar heat load by shade and suitable clothing ; and it is possible to avoid sunburn by simple precautions. The rôle of the sun in heat disease is thermal only ; there is no specific " sunstroke effect." The biological success of the negro in the tropics cannot be attributed to his pigmentation ; because of the pigment the negro absorbs more solar radiation and has a greater total heat load than the white man under similar conditions ; he is, however, less sensitive to sunburn.

*W. S. S. Ladell.*

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## MISCELLANEOUS DISEASES.

HYMAN, A. S. **Heart Disease in the Jungles of the South Pacific : some Observations made among Melanesians of the New Hebrides and Solomons Islands Area.** *Ann. Intern. Med.* 1945, May, v. 22, No. 5, 639–52.

The author, who is well known as a cardiologist, took advantage of an opportunity of examining Melanesian labour recruits to study cardiac disturbances among them, and has written a paper of much interest. He found the incidence of arteriosclerosis to be unduly high, as compared with European and American subjects. The men seemed to be " old at fifty " and in many over 30 years of age, tortuous temporal arteries were observed and radials were thickened. Blood pressure varied in a peculiar way in different localities ; in some the levels were low, 80–90 mm. Hg systolic, and 40–50 diastolic ; but in three islands [they are not specified] high readings up to 236 mm. systolic and 115 diastolic were observed ; in one tribe 11 out of 19 persons over 30 years of age had high pressures and one boy of 18 years gave readings of 160 and 104 respectively. Six out of nine with high pressure gave a history of previous blackwater fever and among the Native Medical Practitioners—a shrewd body of men—there is a current belief that blackwater fever is often followed by hypertension. Cardiac hypertrophy was another common finding for which no cause could be discovered.

Sinus arrhythmia and extra systoles were fairly frequently met with ; of murmurs the commonest were pulmonary systolic, functional in nature, and next apical systolic, also classed as functional as no concomitant signs of heart disease were discovered. This may have been syphilitic in nature but was not so determined. Chronic coronary disease is common but often unassociated with pain, and even when there is pain it is comparatively slight and bears no resemblance to the acute angina pectoris of Europeans. Examination to

compare the pain threshold of the native with that of the white man revealed no difference in degree. Pain and oedema of the feet are found associated with vascular occlusion of the vessels of the leg and foot, which in turn are thought to be due to infections of the limb sustained in the jungle; varicose veins are commonly seen, even in children, and "may have been due to secondary changes . . . the result of continuous re-infection of the feet by various tropical organisms." [This is purely speculative and calls for further research, as indeed does the whole subject of cardiovascular disease among natives, and it is of particular interest in this region of the South Pacific where such lesions are common in one island but are rarely seen in others close by.]

*H. Harold Scott.*

SANABRIA, A. & PLANCHART M., A. El factor carencial en la cirrosis hepática y en la miocarditis bilharziana. [**The Deficiency Factor in Cirrhosis of the Liver and in Bilharzial Myocarditis.**] *Rev. Policlinica Caracas.* 1945, May–June, v. 14, No. 82, 165–97, 1 chart & 19 figs. [78 refs.] English summary (7 lines).

The authors start with a statement and consideration of the many reputed causes of hepatic cirrhosis which have been brought forward from time to time (race, sex, heredity, alcohol, nutritional and toxic causes, etc.), with quotations from the literature of those who have suggested and supported these various theories. They conclude from all this that in hepatic cirrhosis nutritional deficiency plays an important part and that this deficiency is probably specific. They point out that cysteine and methionine exert a powerful action in the production of healthy liver cells and in preventing necrosis; also that fatty infiltration of the organ is an important precursor of cirrhosis and that choline serves to prevent this. Elsewhere it is stated that cysteine is harmful to the liver and may produce irregular proliferation, but that "cysteine, which in other circumstances provokes necrotic lesions of the liver, is beneficial in the presence of choline inasmuch as the methylic groups resulting from the cysteine and the choline bring about the transformation of it into methionine." Hence the benefit which has been reported in cirrhotic patients from the use of choline chloride, with its lipotropic action.

Again, thiamin plays an active part only when it is converted into diphosphothiamin, and patients with hepatic cirrhosis excrete much larger quantities of thiamin than do normal persons.

Six cases are mentioned and a few details on each are given. Three [perhaps four] had ascites and four enlargement of the liver (in another the liver could not be palpated owing to the tenseness of the abdomen); four were passing ova of *Sch. mansoni*, one had dysentery and two had positive Kahn reactions.

Benefit was reported in all from treatment with a diet of high protein, liver extract, choline chloride and mercurial diuretics, together with a combination of vitamins A, B and D. [An elaborate scheme is presented in which more than a score of arrows point to chronic deficiency of vitamins, and there are several photographs of patients overexposed (in all senses of the term) so that they convey little information. The whole article, to the abstracter at least, savours rather of special pleading and is not very convincing, especially as so much is based on so small a number of cases.] *H. Harold Scott.*

MAYER, J. H. **Chronic Melioidosis. A Case showing Multiple Lesions of Bones, Joints, and Lungs.** *J. Bone & Joint Surgery.* 1945, July, v. 27, No. 3, 479–85, 5 figs. [14 refs.]

This paper describes a case of melioidosis which is of particular interest in that it is the second to be reported in a European—a British soldier—and that

it ran a chronic course ; the majority end fatally in a few days or weeks. This case has already been reported by MAYER and FINLAYSON [this *Bulletin*, 1944, v. 41, 694]. The present account adds little to what has already been published. *S. P. Bedson.*

ÖZTURK, M. H. Ueber einen Fall von Morbus Behçet. [**A Case of Behçet's Syndrome.**] *Ophthalmologica.* 1944, Dec., v. 103, No. 6, 288–92.

The patient, a man aged 36, was under observation at a hospital in Istanbul from June to October 1943 ; he gave a history of having had recurrent attacks of the syndrome during the preceding four years. At the hospital he was examined clinically by doctors of several special departments, and various laboratory tests were made.

The symptoms were typical of the disease except that only one eye—the right—was involved, the left remaining unaffected throughout the course of the disease.

Cerebrospinal fluid was injected into two rabbits and three guineapigs, into the anterior chamber of the eye, into the conjunctiva, intravenously and intraperitoneally, with negative results.

Treatment with vitamins $B_1$ and C and sulphonamides had no effect.

No cause was found ; virus-like elementary bodies have repeatedly been seen in Giemsa-stained smears of the aphthae in the mouth. The diagnosis is made difficult by the fact that the three chief symptoms—aphthous ulceration in the mouth, ulceration of the external genital organs, and the eye lesions (conjunctivitis, corneal opacity, hypopyon, hyphaemia, glaucoma) do not appear simultaneously but in irregular order in different cases. [See also this *Bulletin*, 1944, v. 41, 780.] *J. F. Corson.*

VAUGHN, A. M., HOWSER, J. W. & SHROPSHEAR, G. **Ainhum (Dactylolysis Spontanea). Report of Two Cases from Illinois.** *Ann. Surgery.* 1945, Nov., v. 122, No. 5, 868–77, 8 figs. [10 refs.]

BERKOWITZ, S. **Caterpillar Dermatitis.** *Bull. U.S. Army Med. Dept.* 1945, Oct., v. 4, No. 4, 464–7.

A species of caterpillar was found to be the cause of attacks of urticaria among the troops in New Guinea, which sometimes almost reached epidemic proportions. It occurred again in Northern Australia and was investigated. The caterpillars were allowed to crawl on the arms of 15 volunteers ; some developed local urticaria within a few minutes and this was replaced after 3 or 4 hours by a pruritic papular eruption which lasted for several days. Others had a discrete papular eruption which appeared after 6 hours and lasted for a few days to a week or longer. Similar reactions were produced by rubbing the skin with the cocoons or the tuft of hairs at the tail of the female moth. When extracts of the caterpillars were placed on the skin no reaction occurred unless the skin was scarified, and patch tests with filtrates of extracts were negative. Caterpillar hairs soaked in various liquids for 24 hours still caused reactions as did baked hairs also, but not hairs which had been pounded in a mortar.

It was found from these experiments that the dermatitis is produced by the inoculation by means of barbed hairs of an unknown irritant. The Australian caterpillar concerned is *Ochrogaster contraria* ; the name of the New Guinea caterpillar is not given. [See also this *Bulletin*, 1923, v. 20, 801 ; 1933, v. 30, 317 ; 1936, v. 33, 489.] *J. F. Corson.*

## GENERAL PROTOZOOLOGY.

KISKADDON, R. M. & RENSHAW, R. J. F. **Human Coccidiosis.** *J. Amer. Med. Ass.* 1945, July 7, v. 128, No. 10, 731–2, 1 fig.

In the stools of a man aged 60, suffering from ulcerative colitis, certain double-contoured cysts, measuring on an average 10×7 microns, were discovered. The contents of the cysts were a granular protoplasmic material which showed no signs of further development, though observed for months. The authors refer to the structures, one of which is shown in a microphotograph, as cysts of *Isospora hominis*. [It is possible that they are undeveloped sporocysts of this parasite, but without evidence of their further development it is not justifiable to make even a diagnosis of coccidiosis, much less one of *I. hominis*.] *C. M. Wenyon.*

KEAN, B. H., & GROCOTT, R. G. **Sarcosporidiosis or Toxoplasmosis in Man and Guinea-Pig.** *Amer. J. Path.* 1945, May, v. 21, No. 3, 467–83, 5 figs. on 2 pls. [41 refs.]

Cases of sarcosporidiosis in man fall into two groups. The first comprises those in which the parasite is large and enclosed by a striated capsule. The relatively large sporozoites are in groups separated from one another by septa. The characters are those of such well known sarcosporidia of animals as *Sarcocystis tenella* and *S. miescheriana*. The second group includes those in which the parasite is smaller, while the limiting membrane is thin and not striated. The sporozoites are smaller than those of the parasites of the first type and are not separated into groups by septa. The first case in which the parasite was of the second type was one discovered by Darling in 1909 in Panama. He realized that the parasite differed from the typical sarcosporidia, but attributed the differences to the influence of an unusual host, which man was considered to be. He fed guineapigs on infected mouse tissues and subsequently found similar modified parasites in these animals. The present paper describes the case of a woman in whom parasites of the second type were found in the heart muscle, and also records the discovery of similar forms in guineapigs which had not been subjected to experiment. It is concluded by the authors that in Darling's experiments the natural occurrence of parasites in his experimental guineapigs had not been excluded, so that it is more than doubtful that the parasites seen in the guineapigs represented modified mouse parasites. In the guineapigs, parasites were found by the authors in the brain and kidneys as well as in the muscles. It is concluded that the cases in which the parasites are of the second type are more probably instances of toxoplasmosis than of sarcosporidiosis. In the absence of serological and inoculation experiments a final classification of the parasites cannot yet be made.

*C. M. Wenyon.*

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## GENERAL ENTOMOLOGY.

MADDEN, A. H., LINDQUIST, A. W. & KNIPLING, E. F. **DDT Treatment of Airplanes to prevent Introduction of Noxious Insects.** *J. Econom. Entom.* 1945, Apr., v. 38, No. 2, 252–4.

Tests were made in the laboratory, in an artificial cage resembling a part of an aircraft, and in aircraft themselves, of the value of DDT as a residual insecticide. Four types of application were used—aerosols combined with

pyrethrum, dusts, wet sprays and fine mist sprays—and evaluation of the treatments was made at intervals up to nine weeks by exposing mosquitoes and houseflies in treated airplanes for 1½ to 2 hours and counting the insects that were down.

A much more prolonged effect was seen in aircraft with upholstered interiors than in those with an all-metal finish when aerosols and dusts were used [no comparative data are given for wet and fine mist sprays]. In upholstered aircraft the knock-down with different applications was :—

Aerosol (" four or five times the recommended dosage ") 42 per cent. after 3 weeks.

Dust (average dose 2 oz.) 100 per cent. after 6 weeks.

Wet sprays, 5 per cent. DDT, (300 ml. for an average fighter plane) 80 per cent. after 6 weeks.

Fine mist sprays, 20 per cent. DDT, (28 to 35 ml. per plane) practically none after 3 weeks.

Fine mist sprays, 20 per cent. DDT, (400 ml. per plane) complete knockdown after 12 days.

The authors conclude that DDT is a useful adjuvant to normal spraying, which it should greatly reinforce, but not replace. *G. Macdonald.*

Lindquist, A. W., Travis, B. V., Madden, A. H., Schroeder, H. O. & Jones, H. A. **DDT and Pyrethrum Aerosols to control Mosquitoes and Houseflies under Semi-Practical Conditions.** *J. Econom. Entom.* 1945, Apr., v. 38, No. 2, 255–7.

——, Madden, A. H., Wilson, H. G. & Knipling, E. F. **DDT as a Residual-Type Treatment for Control of Houseflies.** *Ibid.* 257–61.

——, Wilson, H. G., Schroeder, H. O. & Madden, A. H. **Effect of Temperatures on Knockdown and Kill of Houseflies exposed to DDT.** *Ibid.* 261–4.

Temperature exerts a marked effect on the rate of knock-down and the final mortality of flies exposed to treated surfaces. When exposed at a temperature of 70°F. and transferred after being knocked down to a temperature of 80°F. to 100°F. they recover, collapsing again when put back in a cooler climate and again recovering if warmed, an alternation which can be repeated several times before death ensues. Similarly, the time in which knock-down occurs varies directly with the temperature, being more than twice as long at 95°F. as it is at 50°F. Flies which had been in contact with a film at a temperature of 70°F. never recovered if subsequently held at that temperature, but some became active within an hour if they were moved to a temperature of 95°F. or 100°F., under which conditions the final mortality was usually less than 100 per cent., and this type of relationship between efficacy and temperature was shown to hold good under a variety of circumstances.

A solution of 5 per cent. DDT and 5 per cent. cyclohexanone in deodorized kerosene (*Deobase*) gave uniformly better results, in terms of knock-down and mortality, than a 5 per cent. solution in kerosene, while solutions in dibutyl phthallate were inferior to those in kerosene.

Solutions and emulsions of DDT applied to screencloth at the rate of 100 mg. per sq. ft. gave satisfactory mortality among insects brought into contact with it, and did not injure the synthetic screencloth used in U.S. services ; the effect of emulsions lasted longer than did that of solutions in kerosene or dibutyl phthallate.

Tests of the efficacy of DDT on different types of surfaces showed that suspensions had a higher toxicity when applied to " inside " paint than on unpainted wood, and had least effect on full oil or " outside " paint. Kerosene solutions were relatively ineffective on any painted surface. DDT mixed with

cold water paints, such as calcimine, and applied at the rate of 25 mgm. per sq. ft. gave a slower knockdown than kerosene solutions applied to the surface, but remained effective throughout the test period of 44 days.

In the first paper the authors record the results of an enquiry into the practicability of substituting DDT for pyrethrum in apparatus of the pyrethrum-freon-aerosol type, but much of the value of the work is lost as a result of their inability to quote the exact formulae used. DDT was found to be insufficiently soluble in *Freon*-12 to provide a satisfactory concentration without the use of an auxiliary solvent, for which purpose cyclohexanone was found most suitable. When DDT was used at concentrations 12·5 times as great as used for pyrethrins, the two were equally toxic to mosquitoes. Good results were obtained when they were combined in unstated proportions, and they were improved by the addition of motor oils of various, unstated, viscosities. *G. Macdonald.*

BLAGOVESCHENSKY, D., BREGETOVA, N. & MONCHADSKY, A. **An Investigation on New Repellents for the Protection of Man against Mosquito Attacks.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Oct., v. 39, No. 2, 147–50.

This is substantially the same paper as that abstracted in this *Bulletin*, 1944, v. 41, 1069.

DE MEILLON, B. & LAVOIPIERRE, M. **New Records and Species of Biting Insects from the Ethiopian Region.** *J. Entom. Soc. Southern Africa.* 1944, v. 7, 38–67, 5 figs.

An abstract of this paper appears in the *Rev. Applied Entom.* Ser. B. 1945, Oct., v. 33, Pt. 10, 153.

GASCHEN, H. Phlébotomes de Suisse. [*Phlebotomus* **in Switzerland.**] *Acta Tropica.* Basel. 1945, v. 2, No. 2, 137–54, 8 figs. [15 refs.]

No study of *Phlebotomus* in Switzerland has been published since GALLI-VALERIO discovered a specimen of *P. papatasi* at Orbe (Vaud) in 1912; when this was pointed out by the present author to the Swiss Entomological Society he received a collection of 20 specimens which were caught at Ascona (Tessin) from June to August 1944.

Two species were identified: *P. perniciosus* (Newstead 1911), male and female, and *P. parroti* (Adler and Theodor 1927), male only. These are described, with drawings of the genital armatures and wing of the former species and of the genital armature and the buccal armature of the latter.

*J. F. Corson.*

PARROT, L. & MALBRANT, R. Notes sur les Phlébotomes. XLVII. Phlébotomes du Moyen Congo. [**Phlebotomus of the Middle Congo.**] *Arch. Inst. Pasteur d'Algérie.* 1945, June, v. 23, No. 2, 121–7, 4 figs.

PARROT, L., MORNET, J. & CADENAT, J. Notes sur les Phlébotomes. XLVIII. Phlébotomes de l'Afrique Occidentale Française. I. Sénégal, Soudan, Niger. [*Phlebotomus* **of French West Africa; Senegal, Sudan, Niger.**] *Arch. Inst. Pasteur d'Algérie.* 1945, Sept., v. 23, No. 3, 232–44, 5 figs. [32 refs.]

## LABORATORY PROCEDURES.

ATCHLEY, J., BACON, R., CURRAN, G. & DAVID, K. **A Clinical Evaluation of the Copper Sulfate Method for measuring Specific Gravities of Whole Blood and Plasma.** *J. Lab. & Clin. Med.* 1945, Oct., v. 30, No. 10, 830–38.

A simple method of determining haemoglobin, haematocrit and plasma protein values from the specific gravities of whole blood, plasma or serum with

the help of charts was proposed by PHILLIPS *et al.* [see *Bulletin of Hygiene*, 1944, v. 19, 140]. The present authors have tested its suitability for hospital practice.

The copper sulphate solutions were in 50 cc. amounts with specific gravities ranging from 1·008 to 1·075 by differences of 0·002 ; when 50 drops of plasma were added to these 50 cc. amounts the average lowering of the specific gravity was found to be 0·0005.

The constancy of the results was tested by determinations by two analysts of specimens of blood from 50 unselected patients in the medical wards ; the results were sufficiently uniform for clinical work. The specific gravity determined by the copper sulphate method was compared with the determinations by the falling drop method of BARBOUR and HAMILTON (*J. Biol. Chem.*, 1926, v. 69, 625) and it was found that the agreement between the two methods was practically as close as between duplicates by either method. The serum protein determination was checked by the Kjeldahl method ; in 12 out of 14 cases there was agreement within ±0·5 gm. per 100 cc., the other two showing differences of +0·7 and −0·8 gm. respectively.

In normal and most pathological blood an approximate calculation of the haemoglobin can be made from the whole blood specific gravity alone if the mean normal value of the specific gravity of plasma is assumed to be 1·0264. In 47 of 50 cases the results were within 1·5 gm. of the figures obtained from the specific gravities of both whole blood and plasma, and except in gross hyperproteinaemia, the specific gravity of whole blood alone may be used to determine the haemoglobin and is reliable within ±2 gm. per 100 cc.

The haematocrit values obtained from the specific gravity were compared with the direct determinations by the centrifuge ; the standard deviation between the two sets of haematocrit values in the authors' patients was ±2·6 cc. of cells per 100 cc. of blood, whereas that for the normal blood specimens of Phillips *et. al.* was only ±1·2. ASHWORTH and ADAMS [this *Bulletin*, 1942, v. 39, 164] found the mean deviation of gravity-calculated haematocrits from centrifuge haematocrits to be three times as great in series of pathological blood as in series of normal blood specimens ; in 51 of 53 cases the present authors found the gravity-calculated haematocrit values to be within ±4·4 cc. per 100 of the centrifuge values ; the other two cases showed deviations of +9 and −8 cc. respectively. A preliminary comparison of gravity and centrifuge haematocrit values would exclude this 4 per cent. of large deviations and then the gravity method could be used afterwards during the clinical course of the disease.

It was found that red cell counts could not be estimated sufficiently accurately from the haemoglobin in cases of anaemia ; for normal blood the equation is : millions R.B.C. per cu. mm.=Hb. (gm. per cent.)×0·325. If the colour index is normal the rapid gravity method may be used to estimate changes in the cell counts during treatment.

The other equations are as follows :—

1. Gm. protein per 100 cc. plasma $= 389{\cdot}6\ (G_P - 1{\cdot}0079)$
2. Gm. Hb. per 100 cc. blood $= 33{\cdot}9\ \dfrac{G_B - G_P}{1{\cdot}0970 - G_P}$
3. Gm. Hb. (approx.) per 100 cc. blood $= 480\ (G_B - 1{\cdot}0264)$
4. Haematocrit (cc. cells per 100 cc. blood) $= 100\ \dfrac{(G_B - G_P)}{1{\cdot}0970 - G_P}$

$G_B$, $G_P$ = specific gravity of blood and plasma respectively.

*J. F. Corson.*

## REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

KARK, S. L. & KARK, E. **The Practice of Social Medicine.** *Clin. Proc.* Cape Town. 1945, July, v. 4, No. 5, 284–307.

The principle of the Health Unit in countries in which the standards of the people are low, or in which rural hygiene is rudimentary, are not new, but have not yet been as widely applied as they could be. The Unit with which the authors are connected was instituted at Polela, Southern Natal, in 1940 [see this *Bulletin*, 1944, v. 41, 611] and has now extended its activities so that 720 homes, comprising about 5,000 people, are constantly visited by, and have become well known to, the staff.

The objects to which those who undertook this venture set themselves were not confined to the treatment and prevention of disease as those matters are generally understood by clinicians and public health workers. The element of social medicine, which involves close study of the homes, economic position, mentality, beliefs and characters of the members of the community, was an essential part of the programme of work. It was not enough to know of the existence of disease and to cure it or to prevent it by public health action ; the disease was rather regarded as one manifestation of a group of events or conditions, and it was held that elimination of that kind of disease in the future would not be possible so long as the basic conditions which gave rise to it, or in which it could flourish, continued to exist. In such public health matters as water supplies and refuse disposal, of course, this line of thought is not new ; what is new in the work of this unit is the fact that attention is paid to many factors beyond those normally considered to pertain to sanitation. In this way, curative medicine and public health activities were combined in one unit which practised social medicine in its full implications ; only thus can that human understanding of the people be achieved which is necessary if medicine is to fulfil its purpose.

The Unit consists of a medical officer in charge, an assistant medical officer, " medical aids," nurses, health assistants and general labourers. It acts in close co-operation with the education and agricultural services in the area, and it conducts clinics, school medical work and routine visits to the homes of the people. In this way, and by constant consultation and pooling of information, the home backgrounds become well known, and the characters, habits, economic standards, movements and inter-relationships of the people are studied. Instances of the bearing of these factors on the health of adults and children are given in the form of detailed descriptions of homes and persons belonging to three families. The people are often illiterate and are strongly attached to belief in witchcraft. They are often lazy and make little attempt to improve their condition ; they misuse their land, with the result that soil erosion occurs and crops are poor ; malnutrition is therefore common. The men are often compelled to leave their homes for long periods, to earn money in the towns, but some of them do not use the money to support their families. Alcoholism is common. In such circumstances there is considerable apathy and resistance to change of habits ; by its educational and medical activities the Health Unit is gradually breaking down this poor and static mentality, but the difficulties are very great.

[To the reviewer it seems that the work of this Unit is admirably conceived. It must in time show to the people that the staff of the Unit has an interest in the welfare of each person as an individual, and it will gradually prove to them that the superstitions to which they are now so firmly attached have no basis in fact. This process will, no doubt, be slow, but there is no valid reason why Africans should be more unable than others to rid themselves of such ideas.

The transition from an old tribal organization, with its clearly understood loyalties and objects, to a more modern and critical community, must be painful and disappointing in that the removal of beliefs leads to cynicism unless they are replaced by progressive ideas equally strongly held. One of the most important of these ideas must be that the individual is valuable to the community, and that the community welcomes whatever contribution the individual can make, and is concerned to maintain the dignity of the individual. Here medicine impinges on the field of political psychology and organization, as much as on that of economics. Medicine must more and more strongly insist that the health of the people depends to an enormous extent upon their mentality and economic status ; that these in turn depend upon the level of general (and not only medical) education and political status, improvement in which entails active co-operation between government and people for the benefit of both ; and that if any one section of a population regards the protection of its health as a human right, there can be no valid reason why that right is not common to all sections. There are indications that the South African Government appreciates the force of such arguments and that it is prepared to act upon them by the inauguration of schemes in which the state of mind of the African is given its proper importance, and by which his economic status will be improved, so that he will take a personal interest and pride in his own progress and welfare.] *Charles Wilcocks.*

Pinto, C. Um ano de combate às doenças parasitárias que atacam os rodoviários da estrada Rio-Bahia, 1942 a 1943. [**Parasitic Diseases in the Labourers on the Rio-Bahia Road. One Year's Experiences during 1942–43.**] *Mem. Inst. Oswaldo Cruz.* 1944, June, v. 40, No. 3, 209–340, 39 figs. & 12 pls. (11 folding). English summary.

The service created to cater for the people engaged in this road work was of considerable scope, and comprised a central laboratory and an emergency hospital, with transport for the sick. The organization is described in detail, for which the original should be consulted.

The chief diseases encountered in these labourers were malaria, schistosomiasis, yaws, amoebiasis, hookworm infestation, scabies and the common infectious diseases. The commonest malaria parasite was *Plasmodium vivax*, but *P. falciparum* was also often found, and *P. malariae* infections are now reported for the first time from the State of Minas Geraes. Experiments on the control of spread of *Schistosoma mansoni* were made by the use of extracts of the stems or fruit of certain saponin-containing plants (*Serjania*, *Sapindus saponaria*), which contain 14 and 12·4 per cent. of saponin respectively. These extracts are fatal to snails (*Australorbis glabratus*) and cercariae within a few minutes. An experiment to infect the hairy armadillo *Euphractus sexcinctus* with *S. mansoni* was successful. This animal was found to be naturally infected with *Ancylostoma caninum.* *Charles Wilcocks.*

González, R. D. Algunos datos sobre la patología de la región de Tingo María. [**Notes on Disease in the Tingo Maria District, Peru.**] *Rev. Méd. Peruana.* 1945, Feb., v. 18, No. 194, 33–68, 4 figs. [16 refs.]

Helminthic infestation is very rife ; according to the hospital laboratory records the incidence is 100 per cent. The commonest worms are *Ancylostoma duodenale*, *Trichuris trichiura* and *Ascaris lumbricoides* ; one-third of the children are sent to the hospital by their mothers with a history of having vomited *Ascaris*. It is frequent to see 8–10 ova of hookworm and *Trichuris* in every field of the microscope. Intense hypochromic anaemia is common, with

red cells down to 1½ million per cmm. and haemoglobin 0·8 gm. per cent. Oedema and pallor accompany this, together with shortness of breath, worse on slight exertion. Dermatitis, especially interdigital, is often observed in cases of ankylostomiasis. Cestode infestation is rare; bilharziasis is occasionally seen in Asiatics from Pampas del Sacramento.

Of protozoal infections espundia is occasionally seen, but no visceral leishmaniasis. Other protozoa met with, but not very often, are *Giardia intestinalis*, *Chilomastix mesnili* and *T. vaginalis*; *E. histolytica* also [incidence not mentioned], *Endolimax nana* and *Iodamoeba bütschlii*. Isolated cases of malaria occur, introduced from without. Locally, no *Anopheles* have been found, though they have been looked for.

Deficiency diseases are seen; this ought not to be since the soil is fertile and the people agricultural. Tropical ulcers are common at all ages in children and adults, mostly with spirilla and fusiform bacilli. Treatment by arsenicals has given good results provided the patients were taken into hospital, but the treatment strongly advocated by the author is cleaning the ulcer with soap and water and then applying a "plaster bandage," 3–4 cm. in width, each fold covering half of the one below, but not so tight as to impede circulation and cause swelling of the limb. If there is much discharge the application may need changing in 3–5 days at first, later every 10–12 days, when epithelization will be found to have started. This, states the author, has proved efficacious in 95 per cent. of cases.

Among 10,000 patients attending the hospital the author has not seen a single case of autochthonous yaws; the few he has seen have all come from other districts. Cutaneous myiasis (*Dermatobia*) is not uncommon and there is a condition known locally as Izangos, due to penetration by a red-bodied Acarine setting up a form of dermatitis. Pinta is occasionally met with. Tarantula bites are much dreaded; the author treats them by intravenous injections of calcium gluconate. It has been believed that *Latrodectus* also exists there, but the author has not yet met with one.

Special mention is made of a disease whose nature is quite obscure. It goes by the name of *Forty-day Fever*. The temperature remains about 38–40°C. for this time, with loss of appetite, rapid respiration, insomnia and increasing debility. The red corpuscles and haemoglobin are not affected, but leucocytes fall to 4,500–5,000 in the early days and after a week or so to 2,500 per cmm. with relative mononucleosis. It is commonest in young adults and in the winter and spring, very rarely is a case seen at other times. Some of the patients present ideas of persecution and show signs of terror; they refuse medicine and are difficult to control, but the majority retain their normal faculties unaffected. The cause is at present quite obscure; no fatal case has yet been recorded.

*H. Harold Scott.*

Connell, W. K. **The Surgical Uses of Zipp.** *Glasgow Med. J.* 1945, Sept. & Oct., v. 26, Nos. 3 & 4, 65–80; 105–15. [35 refs.]

The author gives an introductory account of the steps which led him and Buchanan to introduce Zipp [this *Bulletin*, 1934, v. 31, 337] and then discusses its possible mode of action, in the investigation of which he was assisted by two chemists and a bacteriologist; he concluded from an experiment that ultra-violet rays penetrate plaster of Paris [$CaSO_4$] and set free iodine from the iodoform and that this gives the dressing its antiseptic quality. Zipp differs from Bipp in being entirely non-toxic, an important point in cases where it should be freely applied.

Details of its use for wounds and open fractures are given; as a surgical specialist during the war in East Africa the author treated 101 open fractures

with Zipp, 37 being gunshot wounds [and in almost all, no doubt, plaster of Paris casing was also applied]. Only one patient died, a case of comminuted fracture of the femur which was treated with a Braun splint and skeletal extension. The average time taken to heal (the first 55 cases) was 60 days. None developed tetanus, gas gangrene, iodoform poisoning, myiasis, severe dermatitis, or a repulsive stench. Details are given of a remarkably successful result in a badly smashed forearm which the patient refused to have amputated.

Other conditions in which Zipp has given good results are—soft tissue wounds, abscesses and fistulae, and tropical ulcers; of 183 cases of tropical ulcer fully recorded, 182 healed, the average time being 36·6 days, but the author remarks that by no means all series of Zipp-treated ulcers would have such favourable results. The absence of smell is one of the most pleasing features of the method. The only objection to Zipp in the treatment of fractures is that it is opaque to X-rays; the opacity, however, is only at the fracture site, and in the preliminary cleaning of the wound (*épluchage* and *débridement*) the surgeon would see the site and any metallic foreign bodies, while a second attempt at reduction of deformity should not be made as it is dangerous in such cases. After a few weeks the opacity disappears. [See also this *Bulletin*, 1945, v. 42, 228.] *J. F. Corson.*

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## BOOK REVIEWS.

Nicholls, Lucius [M.D., B.C., B.A. (Cantab.), Director of Bacteriological and Pasteur Institutes & Director of Division of Nutrition, Ceylon, etc.]. **Tropical Nutrition and Dietetics.** Second Edition, Re-written and Enlarged. pp. xii+370, 15 graphs & 32 figs. (19 on 11 pls.). 1945. London: Baillière, Tindall & Cox, 7 and 8 Henrietta Street, Covent Garden, W.C.2. [27*s.* 6*d.*] [Review appears also in *Bulletin of Hygiene.*]

India, together with Ceylon, have contributed so largely to the study of nutrition in tropical regions that it is a pleasure to welcome the second edition of this book. Dr. Lucius Nicholls is the Director of Nutrition in Ceylon and the author of several papers on malnutrition. The second edition has been considerably enlarged: there have been added tables of analysis of foodstuffs, diets have been suggested for institutions, and there are notes on food poisoning and insect pests.

On the whole the book is a clear presentation of the facts of nutrition as they affect the inhabitants of the tropics, especially those who live in Asia. Those who live in Africa and the tropical parts of America, the Pacific islands and the East Indies are rather passed over; but this indeed is just, for far less work in nutrition has been done in these areas and it is only on published data that any author can draw.

The study of nutrition and dietetics has advanced considerably further in the temperate regions of America, Europe, Australia and South Africa than has the study of the same subjects in tropical regions, and it has become a matter of great difficulty, and indeed uncertainty, to know how far the results obtained in the temperate regions can be applied to the tropics. Taken as a whole, those who have studied dietetics in the tropics consider that the inhabitants of these regions do not require as many calories or as much protein, mineral salts (except sodium chloride) or vitamins as are required in temperate regions. Some are positively parsimonious in the amounts which, they suggest, are required in warmer climates and by other races; at the other extreme another

group follows with too little discrimination the results established in temperate regions. Nicholls adopts a position mid-way between the two and if the reviewer disagrees from certain of the conclusions of the book he wishes to make it clear that Nicholls has behind him a large weight of medical opinion in the tropics.

At present the field of nutrition in temperate regions is dominated by what might be called the " optimal " school of thought. To explain what is meant by this, vitamin C may be taken as an example. It is common knowledge that the clinical disease, called scurvy, is produced only when for many months a person has taken very low amounts of ascorbic acid. After the recognition of this fact the tests for sub-clinical scurvy were refined and it has been recognized that, although there may be no scorbutic haemorrhages, the intake of ascorbic acid may be inadequate to ensure the speedy healing of wounds, and that other morbid conditions may arise. It is unfortunately true that it is quite impossible to say where this state of sub-clinical scurvy fades into normal healthy nutrition, and laboratory tests for saturation with vitamin C are probably artificial and yield fallacious results. Nevertheless, in view of all the known facts, nutritionists in temperate regions have agreed to advise an intake of ascorbic acid sufficiently high to guard against any reasonable fear of a deficiency. With our present spectacles we cannot detect the first signs of wear and tear : that is the case for the " optimal " school of thought. The position of the present reviewer is that we should only lower these standards, fairly reasonably established in temperate regions, to suit the inhabitants of the tropics when original observations, confirmed by several workers, suggest that there are certain racial or climatic variations peculiar to the warmer regions of the earth. It may well emerge that certain food constituents are needed in increased amounts in the tropics, sodium chloride is a case in point, others may be needed in decreased amounts, as calories to supply heat loss, but these estimates must be based on original work conducted in the tropics. If there is not enough food in the tropics to give its inhabitants the diet they require, and there is certainly not enough at the present time, we may bow to necessity but we will never lower our conception of the truth.

Of all the food constituents required by man there is more certain knowledge concerning calorie requirements than anything else. Indeed in the question of calories we need not take the approach of the " optimal " school of thought ; too few calories will mean either loss of weight or inability to do hard work ; too many calories, adequately absorbed, will mean an increase of weight. Hunger and a sense of repletion maintain most of us in a delicately adjusted state of weight equilibrium. Let us see how the author approaches this problem.

The discussion of calorie requirements commences on pages 164–172, where it is broken up into two or three portions, with paragraphs about protein and fat requirements in the middle. Under basal metabolism on page 165 there is no clear statement that B.M.R. depends on surface area ; none of the recognized formulae, such as that of Du Bois, is given, so that B.M.R. cannot be calculated from a knowledge of the surface area which any given weight and height will produce. Nicholls states that a reduction of 10 per cent. in the B.M.R. can be allowed for the inhabitants in the tropics, and indeed some reduction is fairly generally accepted, but no reference is made to original observations on this crucial point. There is no clear reference to the Specific Dynamic Action (S.D.A.) of foodstuffs, usually taken as about 200 calories in temperate regions, which must be added to B.M.R. before the base-line to maintain body weight at rest can be drawn. On page 166 Lusk's estimate of the B.M.R. (no reference attached) is given as 1,680 calories for a 70 kgm. man in temperate regions. Incidentally if the height of this 70 kgm. man is 5 foot 11 inches, then according to the Du Bois formula, B.M.R. (not including S.D.A.) would be about 1,800 calories. The former figure of 1,680 calories is

regarded by the author as too high, and is reduced to 1,500, as most of the smaller races of the tropics are not 70 kgm. in weight. Then follow the suggestions of the League of Nations Report (1936) advocating 2,400 calories for a man or woman living an ordinary life in a temperate climate, but not engaged in manual work. This figure of 2,400 calories is reduced by the author to 2,100 calories (page 172), that is a reduction of 300 calories, although the suggested reduction in B.M.R. for the inhabitants of the tropics (page 166) was only 180 calories. To this figure of 2,100 calories, to cover ordinary everyday living, the author adds 400–500 calories for the work of an " average labourer in the tropics." No comment was offered on the League of Nations Report (1936), given on page 166, concerning the calorie requirements for work, so that unless the mechanical efficiency of the labourer in the tropics is better than that found in temperate regions (usually in the region of 20 per cent., like that of a petrol engine), then these 400–500 calories for work are adequate for 6 hours of light work, or 4 hours of moderate work, or 2 hours of hard work, or 1½ hours of very hard work. Some of us would like to add that in our experience the labourer, too often in the tropics, only does this amount of work, and we have suspected that one of the main reasons is that he does not get enough to eat.

Protein requirements are far more generously dealt with in this book. An allowance of 65 gm. is quoted on page 173, on the advice of a single authority, and appears to be the final conclusion of the author. This conclusion is given as a small sub-section of a discussion on the calorie requirements. Previously the author gives, without comment, on page 166, the League of Nations (1936) recommendation of 1 gm. of protein for 1 kgm. of body weight in the adult. If the average weight of the labourer of Southern Asia is 52 kgm. (page 172), then, in the opinion of the reviewer, 52 gm. of protein would appear adequate. As a matter of fact most of the discussion on protein requirements is given in chapter I, pages 9–23, and it is difficult to understand from this section whether the author feels that the figure of 18·75 gm. of protein (page 14) is grossly inadequate or needs considerable addition. No final opinion is given in chapter I, but one is referred at its end to dietary protein allowances in chapter IX. On referring to this chapter, on page 156, one finds it misprinted chapter XI, but in any case it refers only to condiments and beverages. The reference at the end of chapter I probably refers to chapter XI, pages 167 and 173, but in any case one feels that the question of protein requirements has not been handled as a coherent whole.

The reviewer does not wish to stress the viewpoint of the " optimal " school any further, especially in the less certain field of mineral and vitamin requirements. These are dealt with and their uses discussed in chapters II-VIII. The discussion is good and the facts are carefully recorded. Mention is made of the increased needs for common salt in the tropics ; in subsequent editions it will be possible to discuss the deficiency that arises in heat-exhaustion. The parts concerning calcium are good : the author is of the opinion that an adult in the tropics may require 0·5–0·7 gm. and a child 0·5 gm. The latter is about half the amount usually suggested in temperate regions.

The anaemias found in the tropics are described on page 40 under iron requirements. Their classification on this page according to the colour index and cell diameter is based on a false premise, namely, that the colour index should always be exactly 1·0 and the corpuscular diameter should be exactly 7·2$\mu$. Iron-deficiency anaemia and the liver-principle-deficiency anaemias are classified, and, as Nicholls suggests, these anaemias are frequently combined. The reviewer has suggested that this combination might be called " dimorphic anaemia " ; the name, however, is not important, provided the combination is recognized, but the author ascribes the term " diphasic anaemia " to the reviewer (page 45).

The vitamins are adequately and accurately described. Excellent tables on the analysis of foodstuffs are appended. The sections which deal with public health measures are some of the best in the book ; but more might be added on the dependence of improved nutrition on agriculture, the prevention of soil erosion, the question of rents and methods of land tenure. In urban economy the question of a minimal scale of wages, and of feeding labourers, as well as canteens at factories might all be added.

One hesitates to make suggestions concerning additions to a book, but in future editions it might be wise to add sections on fluid intake (a neglected subject among nutritionists), and infant feeding on the breast or by the bottle. As a clinician the reviewer would welcome a clinical section in which first of all the classical diseases, such as beri-beri and pellagra are described. The modern tendency in books on nutrition is to append pellagra to the section on nicotinic acid ; but this strains the truth, for pellagra is probably always a multiple deficiency disease. After this section on the recognized deficiency states there might follow notes on the less clearly defined conditions, the aetiology of which is unknown or uncertain, *e.g.* cirrhosis, plasma protein abnormalities, crazy-pavement dermatosis, deficiency bowel pattern. These are given, with considerable justification, as " indefinite types of malnutrition " on page 153. As one of these indefinite types there is given Barlow's disease, but infantile scurvy is generally recognized and has a precise picture, aetiology and treatment. The other indefinite types of malnutrition include, " mandama, Kwashiorkhor, culebrilla, Gillan's oedema, pellagroid-beriberi." Those who have been interested in the kwashiorkor (misspelt kwashiorkhor) syndrome of malignant malnutrition in Africa and the West Indies feel that it is probably premature to accord recognition to this syndrome in any textbook. We would like to see the very weighty reasons against its recognition presented fairly : thus mandama (pages 284 and 286) is the name employed in Ceylon for what may be rickets. All the other terms on page 153 refer to the same clinical syndrome, described originally and accurately by Cecily (misspelt Cecil page 153) WILLIAMS on the Gold Coast as kwashiorkor. Future work on this syndrome may reveal that it is a mixture of deficiency states, or that it is semi-starvation, or general malnutrition. Briefly speaking, the difficulties in tropical Africa are very great : the diets are grossly inadequate by any standard, including that advocated in this book, yet little recognized malnutrition is present, though much kwashiorkor exists. Whether it is present, perhaps considerably modified, in Asia must remain as yet an open question. Meanwhile oedema, crazy-pavement dermatosis, diarrhoea (page 152), soapy stools (page 154) and fatty livers (page 154) appear to be common. These are all features of the kwashiorkor syndrome. *H. C. Trowell.*

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